QUARTERLY

THE CHICAGO MEDICAL SCHOOL

VOLUME 8, NUMBER 2 DECEMBER 1946

Let your HEAD take you

(The average American today has a choice of just going where "his feet take him", or choosing wisely the course to follow. Let's skip ahead 10 years, and take a look at John Jones—and listen to him . . .)

"SOMETIMES I feel so good it almost scares me.

"This house—I wouldn't swap a shingle off its roof for any other house on earth. This little valley, with the pond down in the hollow at the back, is the spot I like best in all the world.

"And they're mine. I own 'em. Nobody can take 'em away from me.

"I've got a little money coming in, regularly. Not much—but enough. And I tell you, when you can go to bed every night with nothing on your mind except the fun you're going to have tomorrow—that's as near Heaven as man gets on this earth!

"It wasn't always so.

"Back in '46—that was right after the war and sometimes the going wasn't too easy—I needed cash. Taxes were tough, and then Ellen got sick. Like almost everybody else, I was buying Bonds through the Payroll Plan—and I figured on cashing some of them in. But sick as she was, it was Ellen who talked me out of it.

" 'Don't do it, John!' she said. '*Please* don't! For the first time in our lives, we're really saving money. It's *wonderful* to know that every single payday we have *more* money put aside! John, if we can only keep up this saving, think what it can mean! Maybe someday you won't have to work. Maybe we can own a home. And oh, how good it would feel to know that we need never worry about money when we're old!'

"Well, even after she got better, I stayed away from the weekly poker game—quit dropping a little cash at the hot spots now and then—gave up some of the things a man feels he has a right to. We didn't have as much fun for a while but we paid our taxes and the doctor and—we didn't touch the Bonds.

"What's more, we kept right on putting our extra cash into U. S. Savings Bonds. And the pay-off is making the world a pretty swell place today!"

The Treasury Department acknowledges with appreciation the publication of this advertisement by

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QUARTERLY

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THE CHICAGO MEDICAL SCHOOL

VOLUME 8, NUMBER 2 DECEMBER 1945

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Editorials . . .

ENZYMES

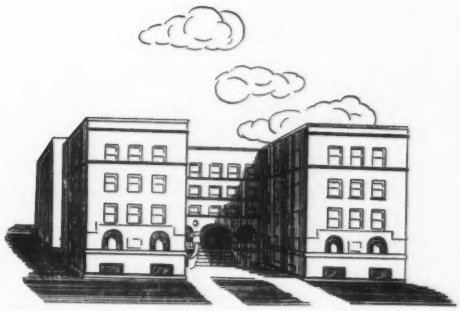
Within the boundaries of metabolism may be considered all chemicals, be they organic or inorganic, which are found in the body as an intermediate or final product of the reactions taking place to maintain a living cytoplasm. With the beginning of modern chemistry an attempt was made to reveal the esotericities of body equilibrium. By analytical studies of the components of various tissues, these early scientists were able to isolate many known chemicals, and by piecing these substances together were able to picture the trend of a reaction. When duplication of this process was attempted in vitro-strong acids, strong alkalis, oxidizing agents, high temperatures and radical pH values were needed. Yet the cell is able to carry out such reactions at approximate neutrality, at body temperature and at high speed. To explain this phenomenon, the chemists had to assume there existed within these tissues catalytic agents — and these were soon isolated — *the enzymes.* However, not until 1926 were the enzymes isolated in pure crystallized form and their true identity revealed.

Dr. James Sumner, professor of Biochemistry at the Cornell University, was born in Canton, Mass., in 1887. He received his A.B. at Harvard in 1910, A.M. in 1913, and Ph.D. in 1914 from the same university. His work in the field of enzymes has been essential and of the utmost importance. His isolation of Urease in 1926 showed for the first time that enzymes could be crystalized in purified form.

Enzymatic research has likewise been the field of endeavor for Dr. John Northrop of the Rockefeller Institute for Medical Research. His early education was received at Columbia. Dr. Northrop succeeded in crystallizing Pepsin in 1930, and during 1946 made known that a mother substance of proteins, called Proteinogen, had been discovered.

According to an announcement on November 14 of 1946, four Americans were awarded the Nobel Prize in physics and chemistry. R. W. Bridgeman of Harvard University was selected for the physics award

for his production of extremely high pressures and his discoveries of the resulting effects of these pressures. J. B. Sumner received one-half of the chemistry award for his distinguished research in the field of enzymology. The second half was awarded jointly to J. H. Northrop and W. M. Stanley of the Rockefeller Institute, Princeton, for the preparation of virus proteins in pure form. In this issue of the Quarterly, we are proud to publish the Nobel Prize Delivery made by Dr. Northrop at Stockholm, Sweden, and an article by Dr. James Sumner on the advancements in enzymology.



With a complete understanding of the mechanisms which enzymes utilize to facilitate chemical reactions, we will gain that much more understanding of protoplasmic metabolism and learn methods for controling organic senescence — if such a thing be possible.

A PLEA

The Quarterly has undertaken the task of giving complete information as to the progress of the school in its attempt to obtain the generous Guarantee Fund for which it is striving. We appreciate the co-operation and donations which have already been graciously added to the steadily increasing fund. But, it is not enough.

The Chicago Medical School has now gained nation-wide recognition for its academic liberalism. Many cities of the United States have representatives telling of the existing uniquness and great potential of the medical college. But it seems that the flame of that people who fought for the Bill of Rights has not reached its kindling point. The realization that true professional educational freedom is now a possibility has not, as yet, struck a resounding chord.

Religious and press freedom was granted to a people starving for the right to live and think as they pleased, yet, there exist a great many highly capable men in this world who are yearning for an opportunity to educate themselves professionally, and find not capability, but other personal qualities hampering them in their vain effort. The desire, on the part of the earnest students, is as strong as that of the Colonists of America when they found themselves hampered by regal and provincial restrictions. This feeling was soon put to force and an equality was created which put man at peace for a while.

Let the same spirit which influenced Americans in days past become once again kindled. Educational freedom is as vital as press freedom and with the help of all we'll overcome the impediments that still hold us back.

THE PREPARATIONS OF PURE ENZYMES AND VIRUS PROTEINS * †

John H. Northrop, B.S., Ph.D. — Rockefeller Institute
Nobel Prize Winner for Chemistry — 1946

THE problem of the chemical nature of the substances which control the reactions occurring in living cells has been a subject of research, and also of controversy, for nearly two hundred years. Before the eighteenth century these reactions

PEPSINOGEN 340x
(*Herriott*)

were considered as "vital processes," outside the realm of experimental science. The work of Spallanzani, Payen and Persoz, Schwann, Kuhne, and finally Buchner proved that many of these reactions could take place without living cells and were probably caused by the presence of small amounts of unstable and active substances, which Kuhne called "enzymes."

Berzelius, a century ago, pointed out that these enzymes were similar to the catalysts of the chemist and suggested that they be considered as special catalysts formed by the cells. This hypothesis was far ahead of its time and met with great opposition, since many workers considered that enzyme reactions differed qualitatively from ordinary chemical reactions. The work of Tamman, Arrhenius, Henri, Michaelis, Nelson, von Euler, Willstatter, Warburg, and other chemists, however, has shown that Berzelius' viewpoint was correct and enzyme reactions are now considered a special kind of catalysis which does not differ qualitatively from other catalytic reactions.

While the study of enzyme reactions made rapid progress all attempts to isolate an enzyme and so determine its chemical nature were unsuccessful until recently.

The early workers were of the opinion that enzymes were probably proteins and in 1896 Pekelharing isolated a protein from gastric juice which he considered to be the enzyme pepsin. He was not able to crystallize the protein and his conclusion as to the identity of the enzyme and the protein was never accepted. I repeated these experiments about 1920 but was unable to carry them further at that time. In the meantime a large amount of work, principally by Willstatter and his students, led to the conclusion that enzymes were a special class of unknown compounds, and certainly not proteins.

However, in 1926, Sumner isolated a crystalline protein from beans which he considered to be the enzyme urease. This conclusion was also received with skepticism but, as you know, it has turned out to be perfectly correct. Professor Sumner discusses this work in this issue of the Quarterly.

Sumner's results encouraged me to take up the pepsin problem again and in 1930 I isolated a crystalline protein from a commercial pepsin preparation which appeared to be the enzyme

* Nobel Lecture read at Stockholm, Dec. 12, 1946.

†A detailed description of the results may be found in *Crystalline Enzymes*, 2nd edition, J. H. Northrop, M. Kunitz, and R. M. Herriott. Columbia University Press, New York, (in press).

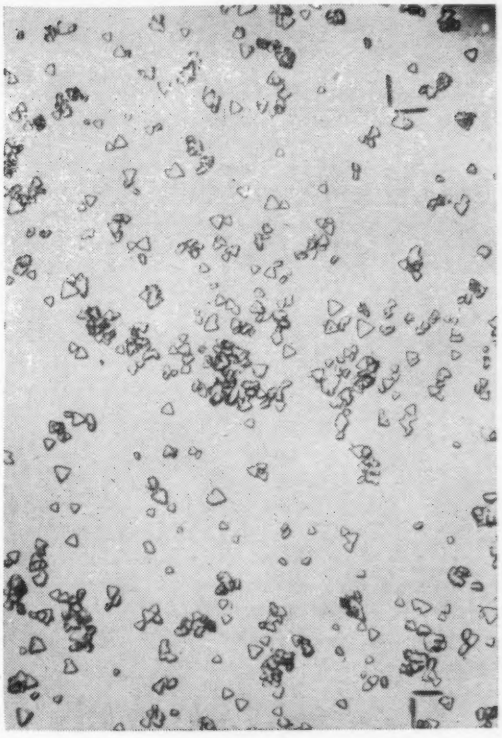
PEPSIN 90x
(*Northrop*)

pepsin. Since then five more enzymes, as well as some of their precursors, have been isolated in my laboratory. Trypsin, and its precursor trypsinogen, a polypeptide which inhibits trypsin, and a compound of this substance with trypsin, chymotrypsinogen, and three forms of chymotrypsin were isolated and crystallized by Kunitz and myself. Kunitz and McDonald isolated and crystallized ribonuclease and hexokinase. Anson crystallized carboxypeptidase, and Herriott isolated and crystallized pepsinogen. These experiments required a great deal of the most painstaking and difficult work and could not have been successfully carried out without my collaborators, Herriott, Anson, Desreux, McDonald, Holter, Krueger, Butler, and, especially, Dr. Kunitz, who possesses a real genius for handling these unstable and elusive substances.

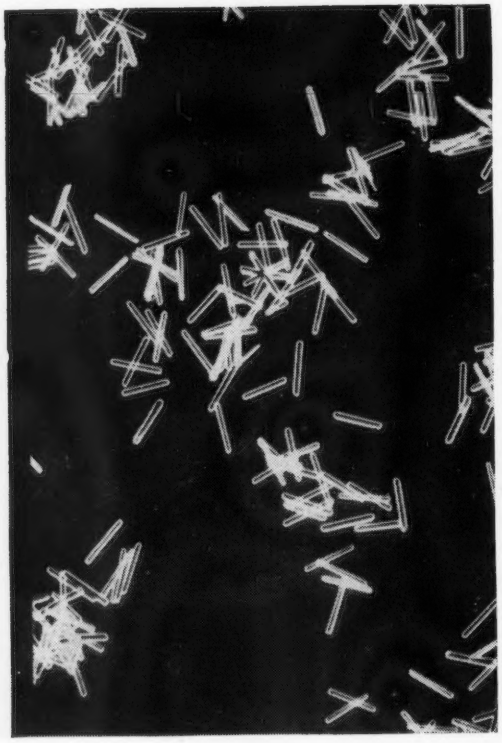
In the meantime some twenty enzymes have been crystallized in all by other workers; all of these enzymes are proteins. The respiratory ferments of Warburg and other oxidative enzymes contain special groups other than amino acids, but the purely hydrolytic enzymes, so far as is known, do not.

While this work was in progress a new controversy, very similar to the old controversy over the nature of enzymes, arose concerning the chemical nature of viruses. Dr. Stanley succeeded in crystallizing the virus of tobacco mosaic and has isolated a number of other viruses. Bawden and Pirie have crystallized the bushy stunt virus of tomatoes. I have isolated a nucleoprotein which appears to be one of the bacterial viruses, or bacteriophages.

As a result of these experiments, it appears probable that all enzymes and at least some viruses are proteins. The mere fact that the preparations are crystalline proteins is not, of course, sufficient to warrant this conclusion and we have spent a great deal of time in establishing the purity of our preparations and in testing by every method available the relation between the activity and the protein.



TRYPSINOGEN 220x
(*Kunitz*)

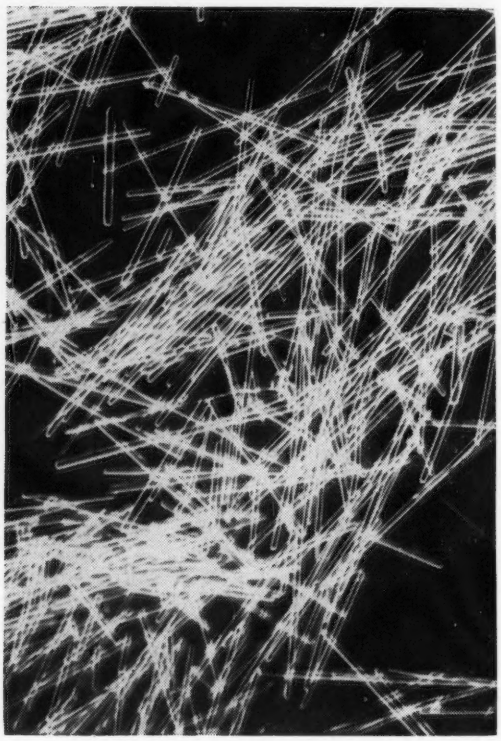


TRYPSIN 202x
(*Kunitz*)

Before discussing these results, I will describe briefly the experimental methods we have used in the isolation and crystallization of these active proteins. No one general method has been found which will lead to the isolation and crystallization of an enzyme, but certain general principles have been found to be of great assistance. In the first place large quantities of material are used, so that actual solid material is handled and not merely dilute solutions. The failure of so many early attempts to isolate enzymes was due, I believe, largely to the fact that nearly all of the work was carried out with dilute solutions. In the second place filtration by suction was used wherever possible since this method results in far better separation of the precipitate from the mother liquor than does the use of the centrifuge. Had Pekelharing filtered his pepsin preparation and then dissolved it in a very small amount of water, instead of centrifuging the precipitate and dissolving it in a large amount of water, I am quite sure he would have crystallized the enzyme nearly fifty years ago.

In the third place fractionation was carried out largely by the use of concentrated neutral salts in the presence of which proteins are much more stable than in dilute salt solutions.

Pepsin, for instance, decomposes at the rate of about 3 per cent a day in hydrochloric acid solu-



CHYMOTRYPSINOGEN 260x
(*Kunitz*)

tion at pH 2.7 and 0°C. Even in nearly saturated magnesium sulfate solutions at 0°C., the most stable condition known, the rate is 1 per cent a day.

Trypsin at pH 8.0 and 3°C. loses 9 per cent or more of its activity in a day. This reaction is exceptional since it is bimolecular so that in this case dilute solutions are more stable than concentrated ones.

Tests of Purity

Solubility.—There is no doubt that the crystalline materials isolated by Sumner, myself, and others are proteins but the proof that these proteins are the enzymes, themselves, is open to question owing to the difficulty of establishing

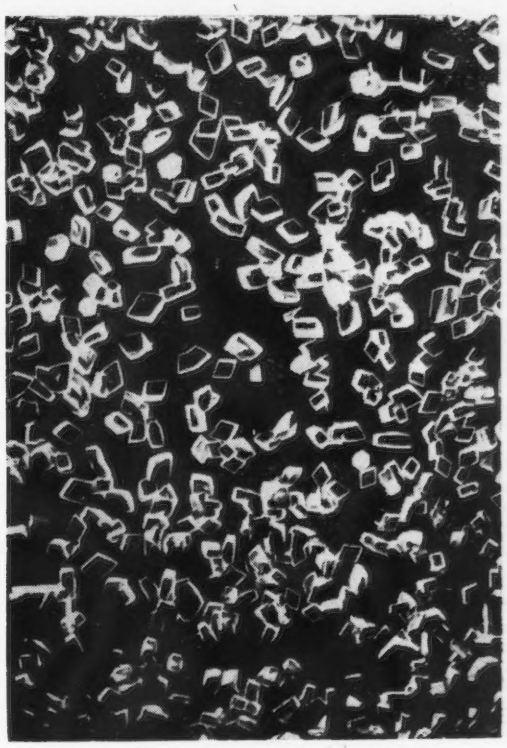
the purity of a protein. In organic chemistry, constant properties, composition, and melting point, through repeated fractional crystallization, are considered as sufficient proof of purity. In the case of proteins, constant analysis means very little and the melting point, which is the most sensitive test, cannot be used since proteins decompose instead of melting. However, the solubility of the protein, which, from the point of view of the phase rule is strictly analogous to the melting point, may be determined instead.

According to Willard Gibbs's phase rule, a system consisting of a single solid in equilibrium with its solution is of fixed composition. That is

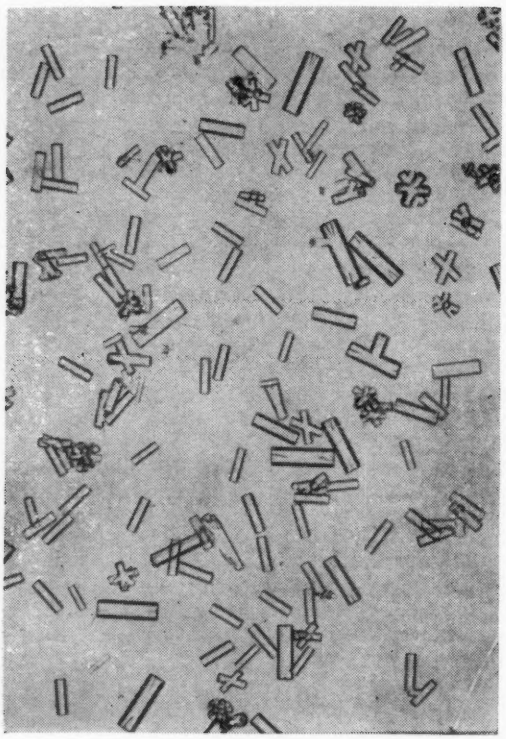
β CHYMO-TRYPSIN 315x
(*Kunitz*)

to say, if more of the same solid is added no change in concentration will occur. If any other substance is added, however, a change will occur. The test is exceedingly specific, even more so than the serological tests as Landsteiner and Heidelberger pointed out. It will, in fact, distinguish between optical isomers, even though the two isomers have exactly the same solubility. In addition, the concentration of the active material as well as the protein may be determined. From the experimental point of view it has the great advantage that the test may be carried out in concentrated salt solution, in which the proteins are most stable. Very few pure proteins have ever been obtained, as judged by this test. Of these, Chymotrypsinogen is probably the best. Pepsin, pepsinogen, chymotrypsin, trypsin, ribonuclease, and hexokinase all give solubility curves closely approaching those of a single substance and as good, or better, than those obtained with most other proteins.

The fact that strictly homogeneous proteins are so difficult to prepare indicates that very closely related groups of proteins, and not one particular individual, are synthesized by the organism. The recent interesting results of Pedersen and of Wyman, Rafferty, and Ingalls, who found that the proteins of young animals differ from those of old animals, confirms this explanation. It is very unlikely that an animal synthesizes the "young"



α CHYMO-TRYPSIN 120x
(*Kunitz*)



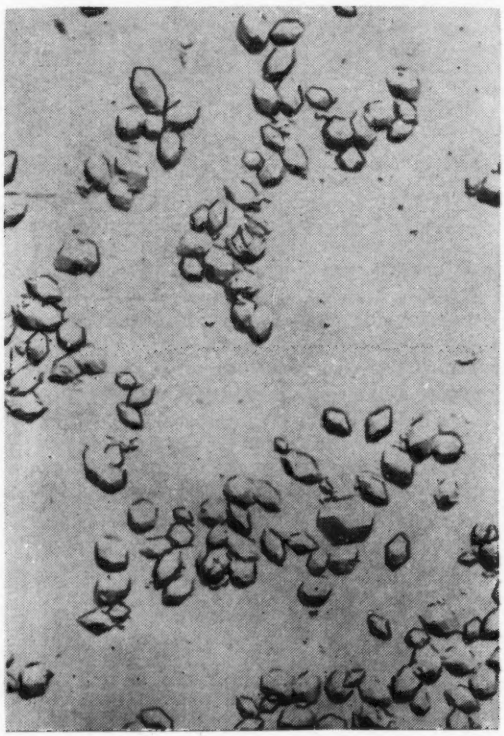
TRYPSIN INHIBITOR 225x
(*Kunitz*)

protein for a certain time and then suddenly synthesizes the "old" protein and hence it is probable that the various kinds of protein are present at the same time in any one animal.

Analysis in the ultracentrifuge.—The many important and striking results which Professor Svedberg has obtained with the ultracentrifuge are familiar to all of you. I need only say that it is a very valuable criterion of homogeneity in protein solution. There is an experimental difficulty in the case of the extremely unstable proteins with which we are involved in that concentrated salt solutions cannot be used owing to their high specific gravity, and some of the proteins are too unstable in dilute salt, even at 0°C., to enable the measurement to be made. Nevertheless, the enzymes pepsin (Philpot and Eriksson-Quensel), ribonuclease and hexokinase (Rothen), and the bacteriophage nucleoprotein (Wyckoff) were found to be homogeneous by this test.

Electrophoresis.—The elegant electrophoresis technique of Tiselius also needs no description in Stockholm. Ribonuclease, hexokinase, and chymotrypsinogen have been examined by Rothen and found to be homogeneous. Tiselius, Hanschen, and Svensson studied the electrophoresis of pepsin and found the main protein component to be strictly homogeneous under a wide variety of conditions, but some inactive nitrogenous material was separated from the protein by this method.

Agren and Hammarsten found that the enzyme migrated to the anode at pH 3.4 and to the cathode at pH 2.7. Tiselius, Henschen, and Svensson, on the other hand, found the protein migrated always to the anode, while I had found by cataphoresis experiments that the protein was isoelectric at about pH 2.4. The electrophoresis experiments were repeated by Herriott, Desreux, Rothen, and Longsworth, using a specially purified pepsin preparation, and both the Tiselius and Theorell apparatus. The experiments showed that the various conflicting results were due to decomposition products in the pepsin prepara-

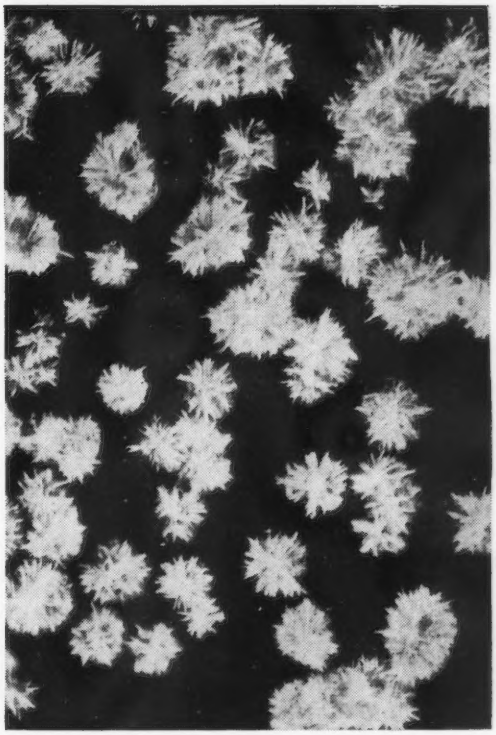


TRYPSIN INHIBITOR
Compound 370x
(*Kunitz*)

tions. In the presence of these products the enzyme has an isoelectric point at pH 2.5 to 3.0, whereas the pure protein has no determinable isoelectric point. This marked effect of hydrolysis products on the electrophoresis of pepsin had been observed many years ago by Ringer. These non-protein decomposition products may be removed partially by electrophoresis but we could find no evidence for the presence of more than one protein by this method.

Agren and Hammarsten were also able to separate crystalline carboxypeptidase into several components, so it appears that this enzyme has not yet been prepared in pure form.

The results of these various tests of purity warrant the conclusion, I believe, that the enzymes pepsin, trypsin, chymotrypsin, hexokinase, and ribonuclease are at least as homogenous as any known proteins. Chymotrypsinogen is probably the purest protein so far isolated. This statement refers only to specially prepared and highly purified samples. The first crystallization usually results in a product which still contains impurities and in some cases more than one protein.

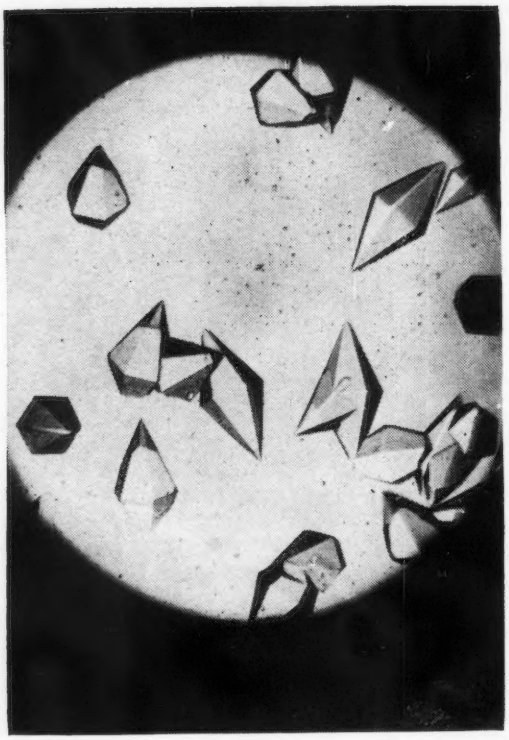


RIBONUCLEASE 190x
(*Kunitz*)

δ CHYMO-TRYPSIN 15.5x
(*Kunitz*)

Relation of the Activity to the Protein by Other Methods

Formation of enzymes from their precursors.— Pepsin, trypsin, and chymotrypsin are derived from inactive precursors. These precursors were isolated and crystallized and the formation of the active enzyme studied. The formation of pepsin from pepsinogen and trypsin from trypsinogen are autocatalytic reactions. These enzymes may, therefore, be "propagated," just as are bacteria. The formation of trypsin from trypsinogen may also be catalyzed by enterokinase, an enzyme of the digestive tract, or by an enzyme produced by a mold (penicillium). The formation of chymotrypsin from chymotrypsinogen is catalyzed only by trypsin, so far as is known. In all these reactions the increase in enzymatic activity is accompanied quantitatively by the appearance of the new enzyme protein which is quite different in all its properties from the original precursor.



ACTIVE ACETYLPEPSIN 34x
(*Herriott*)

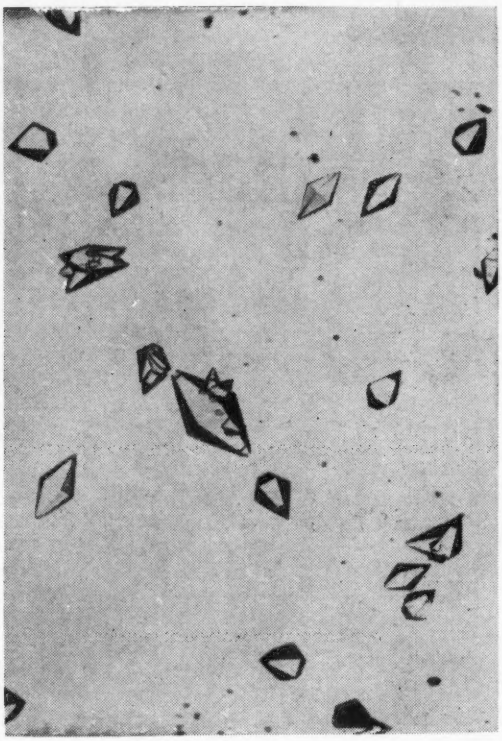
It seems to me that these results are perhaps the most convincing evidence that the enzymatic activity is actually a property of the protein molecule.

Rate of diffusion of the protein and the active substance.—The relationship of the protein and the enzyme may be tested further by measuring the rate of diffusion of the preparation by means of protein determinations and also by enzyme activity measurements. The rate of diffusion was suggested by Arrhenius years ago as a means of determining the size of unknown substances. The method has been developed and used by von Euler.

Theoretically it is simple but experimentally it was difficult. These difficulties were overcome by Anson and myself, who developed a diffusion cell made of a porous disk across which diffusion takes place. This greatly accelerates and simplifies the experiment. The method is the only one, I believe, which permits the estimation of the molecular weight of unknown and impure substances.

The diffusion of pepsin, trypsin, chymotrypsin, chymotrypsinogen, and bacteriophage has been followed by this method. The results show that the protein and the active substance diffuse at exactly the same rate.

Effect of hydrolysis of the protein on the enzymatic activity.—Digestion of trypsin or ribonuclease with pepsin results in loss of activity which is almost exactly parallel to the loss of protein. There is no indication that the protein may be hydrolyzed without also destroying the



ACETYLPEPSIN 60% ACTIVE 28x
(*Herriott*)

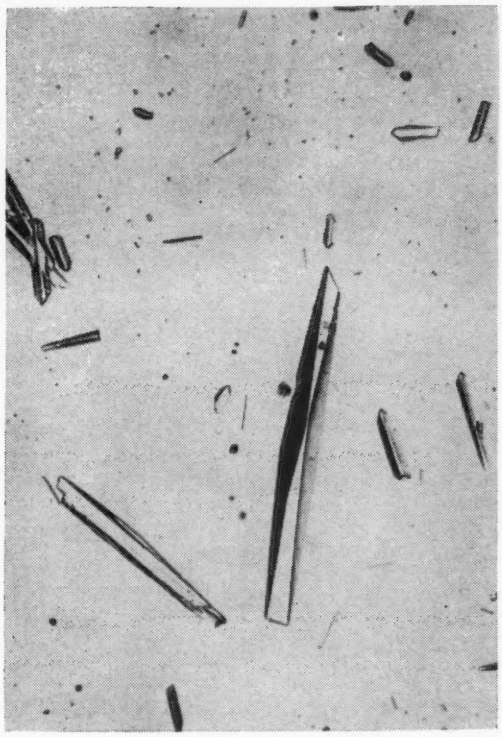
enzymatic activity, nor that any of the hydrolysis products possess measurable activity. Similar results were obtained during the autolysis of pepsin and the digestion of bacteriophage with chymotrypsin.

Denaturation of the protein and loss of activity.—The denaturation of proteins is a characteristic property and has an extremely high temperature

coefficient. The rate of formation of denatured protein and the loss in enzymatic activity has been compared in the case of pepsin, trypsin, chymotrypsin, ribonuclease, and hexokinase. In every case the loss of native protein is accompanied by a concomitant loss of enzymatic activity.

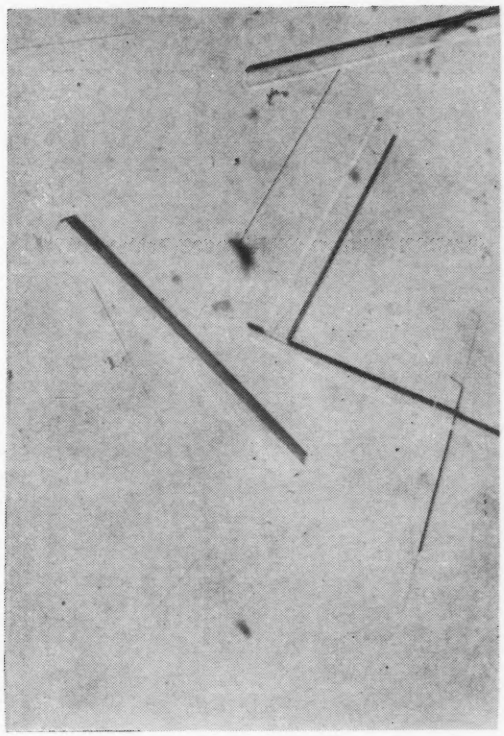
An equilibrium exists between native and denatured trypsin which is accurately predicted by Van't Hoff's equation.

Reversal of the reaction results in recovery of the enzymatic activity in proportion to the recovery of native protein.



CARBOXYPEPTIDASE 85x
(*Anson*)

Effect of chemical changes in the protein molecule on the activity.—Ketene reacts with pepsin to form a series of acetylated products. Herriott has isolated and crystallized three of these derivatives. One contains three or four acetyl groups, probably attached to the primary amino groups. This derivative has the same activity as the original pepsin. A second derivative has about



HEXOKINASE 116x
(*Kunitz and McDonald*)

ten acetyl groups and 60 per cent of the original activity, while the third preparation contains twenty to thirty acetyl groups and is inactive. There is evidence that the acetyl groups which are attached to the hydroxyl group of tyrosine are responsible for the loss of activity. This conclusion is borne out by the fact (Herriott) that iodination of pepsin results in the addition of iodine to the tyrosine groups, and also results in loss of activity.

Pepsin, as well as other enzymes, is also inactivated by mustard gas (dichlor ethyl sulfide). This substance is an excellent protein reagent. It reacts in slightly acid solution with carboxyl groups and probably with the hydroxyl group of tyrosine.

Summary

The enzymes, pepsin, trypsin, chymotrypsin, carboxypeptidase, ribonuclease, and hexokinase have been isolated and crystallized. The precursors of pepsin, trypsin, and chymotrypsin have also been isolated and crystallized. A nucleo-

PEPSIN FROM ALCOHOL 225x
(*Northrop*)

protein which appears to be bacteriophage has been isolated but not crystallized.

The purity of the enzyme preparations, with the exception of carboxypeptidase, has been tested by means of solubility measurements, ultracentrifuge analysis (pepsin, ribonuclease, hexokinase, and bacteriophage), and electrophoresis (pepsin, ribonuclease, hexokinase, chymotrypsinogen). They appear to be pure proteins by all these methods.

The relation of the enzymatic activity to the protein has been tested by diffusion measurements (pepsin, trypsin, chymotrypsin, chymotrypsinogen, bacteriophage), denaturation of the protein (pepsin, trypsin, chymotrypsin, ribonuclease, hexokinase), hydrolysis of the protein (trypsin, ribonuclease, pepsin, bacteriophage), formation of the active enzyme from an inactive precursor (pepsin, trypsin, chymotrypsin), and by the formation and isolation of definite chemical derivatives of pepsin. These experiments confirm the conclusion that the enzymatic activity is a property of the protein molecule, itself, and is not due to a non-protein impurity.

Pioneers of Chemotherapy

The earliest pioneers in the field of chemotherapy came from the ranks of the early bacteriologists and the first recorded chemotherapeutic experiment is attributed to Robert Koch. In 1881, Koch observed the bacteriostatic effects of bichloride of mercury on spores of anthrax cultured in vitro. He worked with gunea pigs, giving them, after innoculation with anthrax spores, injections of 17% sublimate solution bichloride of mercury. Koch reports that despite the sublimate injections, the animals died of anthrax." He concluded, however, that, "I consider this research to be far from complete despite negative results."

So discouraging was the early work that Behring was prompted to state, "It can be regarded almost as a law that the tissues of man and animals are many times more susceptible to poisonous effects of disinfectants than any bacteria known. The pessimism of him who declared that disinfection in the living body is for all time impossible appears to be only too justified."

Progress, however, was made by Behring's own assistant, Oscar Boer when he observed that the bacilli of anthrax and diphtheria were equally susceptible to phenol and mercuric chloride, but methyl violet proved seven times more active against the anthrax bacillus than against diphtheria and thus showed that some disinfectants have a selective action on certain organisms.

Ehrlich, who dominated the early field of chemotherapy, based a good deal of his work on a paper read as a medical student by Emil Heubel dealing with lead poisoning. He was impressed by the fact that the metal preferred certain tissues and did not disseminate evenly throughout the body. He did all his work on dyes and chemicals with this concept in mind.

In 1904 Ehrlich and Shiga succeeded in sterilizing the blood of experimental animals infected with trypanasoma aquinum by injecting trypan red. He did not have similar success with the drug in other animals and though the experiment was of no practical value, it represented the first attempt to create compounds with definite parasitocidal powers.

ENZYMES

James B. Sumner, A.B., A.M., Ph.D. — Cornell University

Nobel Prize Winner for Chemistry — 1946

THE YEAR 1926 is notable in the history of science because it witnessed the preparation in pure form of the first hormone, the first vitamin and the first enzyme. These were, respectively, insulin, crystallized by Abel; vitamin B_1, or thiamin, crystallized by Janson and Donath; and the enzyme urease, crystallized by Sumner. Hormones, vitamins and enzymes occur in all living things. The hormones can be defined as chemical messengers; some are proteins, while others are steroids and one is an amino acid. Vitamins are always relatively simple substances and may be alcohols, aminos, organic phosphates, etc.

Enzymes are the tools of the cell. They cause chemical reactions to go on. They bring about digestion, fermentation, respiration, fertilization, growth and, in fact, nearly every chemical process involved in the phenomenon which we call life. The muscle cell is known to contain 60 different enzymes and probably contains many more which await discovery. Yeast cells doubtless contain a much greater assortment of enzymes than muscle cells, since yeast possesses a greater number of functions to perform.

While all enzymes thus far isolated have been found to be proteins, one class of enzymes, the oxidases, which bring about cell oxidations and produce energy and heat, has been found to consist of compound proteins. Here a protein is attached to a coenzyme. The coenzyme has a relatively simple structure derived from and closely related to a vitamin. From this it has developed that the animal eats vitamins in order to produce coenzymes.

Pure enzymes form microscopic crystals which nearly always belong to either the isometric or to the hexagonal system. Most enzymes in the solid state are colorless, but some are yellow and others are brown. Catalase, isolated from beef liver by Sumner and Dounce in 1937, is brown. With a few exceptions all enzymes are destroyed by boiling. Enzymes that are out of place are dangerous to life. Thus, the venom of poisonous snakes, bees, wasps and scorpions is nothing more than a mixture of many enzymes and when introduced into the body these enzymes destroy tissues with which they come in contact.

The reason why the isolation of enzymes in pure form was so long delayed is because enzymes occur in plants, animals and microorganisms in minute amounts, because enzymes are usually very unstable and because enzymes are colloids, or glue-like substances, whose physical properties require a special type of treatment.

The isolation of urease by Sumner was the first instance of success after nearly 100 years of effort to obtain an enzyme in pure form and to find out what it was chemically. In Germany the noted chemist, Richard Willstatter, and his staff carried out an immense amount of work in attempts to isolate enzymes, but without success. The claim of Sumner of having isolated urease was bitterly contested by members of the Willstatter school and finally admitted to be true only some ten years later. During this interval Professor Sumner made two trips to Sweden for the purpose of obtaining additional evidence supporting his claim. In 1929 he worked in the laboratory of Professor Hans van Euler at Stockholm Hogshule and in 1937 he carried on experiments at Upsala in the laboratory of Professor Svedberg.

Researches in other laboratories furnished powerful support for the isolation of urease. Dr. John Northrop of the Rockefeller Institute was able to crystallize pepsin in 1930 and shortly afterward Northrop and Kunitz crystallized trypsin and chymotrypsin. In Sweden Professor Theorell crystallized the yellow enzyme of Warburg. Recently he has crystallized peroxidase. To date nearly thirty enzymes have been obtained in pure condition by various scientists and today nobody hesitates to accept the pioneer work of Sumner. The importance of enzymes has now been fully realized and many problems in biology are being solved through a study of individual enzymes and those chemical reactions which they either hasten or initiate. One definition of life is: "A proper and orderly functioning of enzymes."

CLINICAL PATHOLOGICAL CONFERENCE

PRESENTED AT THE WOODLAWN HOSPITAL

J. D. Kirshbaum, M.S., M.D., F.A.C.P.
Associate Professor of Pathology
Chicago Medical School

THE PATIENT, a 66-year-old retired government meat inspector, was admitted to the Woodlawn Hospital on the service of Dr C. A. Elliott, on October 18, 1946. The chief complaint was abdominal pain, which had been present for 3 days, and had gradually increased in severity. The day before admission, the patient became stuporous. In 1937, the patient had been hospitalized at Woodlawn Hospital for a heart condition. An electrocardiogram showed myocardial damage, probably on a coronary basis. In 1938 the patient was again hospitalized. At this time, an electrocardiogram disclosed evidence of a bundle branch block, and advanced coronary sclerosis. On admission to the hospital, the patient appeared irrational, and was disorientated. The temperature of 98.4, the respirations were 40, and the pulse was imperceptible. The blood pressure was 80 systolic, and 40 diastolic. The lungs were clear on auscultation, and the heart appeared enlarged on percussion, while the tones were not audible. The abdomen was markedly distended, and there was a generalized tenderness on palpation, and diffuse rigidity.

Clinical Impression:

Shock, due to intestinal obstruction.

Laboratory Findings:

The urine analysis showed a 1 plus albumin, a trace of sugar, numerous hyaline casts, and a few white blood cells.

Blood: Red blood cells, 4,610,000, Hemoglobin, 97%. White blood cells, 13,550. Differential count showed Neutrophilic leucocytes, 66%, Stabs, 10%, Lymphocytes, 23%, Monocytes, 1%.

X-ray Examination: (Dr. Harry A. Olin).

A portable x-ray film, revealed a greatly enlarged heart, while the lungs appeared hazy.

Clinical Course:

The patient was given coramine, plasma, and glucose intravenously. His blood pressure rose to 176/104, but gradually dropped. Because of the dyspnea, oxygen was administered. Dr. H. P. Jenkins saw the patient in consultation, and considered the patient's condition too critical for operation. His impression of the abdominal condition was (1) volvulus, (2) Superior mesenteric vein thrombosis, and (3) acute intestinal obstruction, due to a neoplasm.

Despite the administration of aminophyllin, digifolin, and atropine, the patient became steadily weaker, and he expired on October 19, 1946, about 16 hours after admission to the hospital.

Clinical Discussion:

This patient presents two pathological conditions. One, that he had coronary disease, and secondly, that his present picture indicated an acute abdominal condition.

Since this patient was known to have had heart disease, it is not unusual to see such a patient develop a mesenteric thrombosis, and as a result of this, a hemorrhageis infarction of the small bowel. This complication causes acute abdominal pain, and distention. Other abdominal conditions to be considered in this case, are intestinal obstruction, due to a malignant tumor, acute pancreatitis, or perforation of the gall bladder, a peptic ulcer, or a diverticulum. This man's past history would exclude an empyema of the gall-bladder, or a peptic ulcer. The man's obesity might suggest a pancreatitis. In the absence of any previous laparotomy, there would be little likelihood of a volvulus due to adhesions or bands. The man was in such a critical condition, that exploration was not deemed advisable. The presence of shock was evident by the low blood pressure, and the high hemoglobin indicated the presence of a hemoconcentration of the blood which also confirms the diagnosis of shock. The patient's short illness in the hospital, did not lend itself to a more thorough workup.

Autopsy Findings:

The body was that of an obese white male, weighing 200 lbs. The skin was pale, and the abdomen was markedly distended. There was a pectoral alopecia present. The abdomen contained about 4000cc of a bloody fluid, and the intestines were distended. The lower two thirds of the jejunum, and the upper half of the ileum were discolored deep purple, and the wall was thickened and hemorrhagic, while the lumen was filled

with a bloody fluid. The mesenteric veins, leading to the above segment of bowel, were occluded by thrombi. The thrombi extended into the superior mesenteric vein, and the portal vein.

The heart was enlarged, and weighed 520 Gms. The myocardium was soft, and pale purple grey. The left ventricle measured 28 mm. in thickness, while in the region of the apex, it was reduced to 11 mm., and scarred, especially the posterior wall. The valves appeared normal. The wall of the left coronary artery was thickened, and the intima was covered by fatty and hyaline plaques. The right circumflex branch was thickened and occluded. The aorta showed an advanced atherosclerosis.

The lungs were moderately distended, and on sectioning, showed a passive hyperemia, and numerous, scattered, firm, grey white tumor nodules.

The liver weighed 2620 Gms., almost twice the normal size. It was firm, and on sectioning, most of the right lobe of the liver, was replaced by a homogeneous, grey white tumor tissue. In the remaining parts of the liver, there was an increased fibrosis, and nodular elevations.

The gall bladder was distended, and the serosa was studded with white tumor nodules, that measured up to 10 mm. The bile ducts were free.

The spleen was enlarged, and weighed 260 Gms. The pulp was hyperemic. The kidneys were of normal size, and revealed a passive hyperemia.

In the descending colon, the mucosa presented numerous diverticula.

The right iliac artery was thickened by calcific plaques, and there was a 15 mm. outpouching of the lumen filled with a thrombus.

Microscopical Description:

Sections thru the tumor of the liver, revealed nests and cords of polyhedral-like cells, with large oval and round, hyperchromatic nuclei. There were many atypical mitotic figures present. The structure of the tumor resembled cords of liver cells. In places the tumor showed marked necrosis, and distal to the tumor, the peri-portal septa was thickened by fibrous tissue proliferation, heavily infiltrated with round cells.

In the lumen of the branches of the portal vein, clumps of tumor cells were present. The lobules of the liver cords were frequently interrupted by the fibrous tissue proliferation.

In the lungs, many alveoli were filled with tumor cells.

The lymph nodes were replaced by tumor metastases.

The anatomical diagnosis in this case, was as follows:

1—Primary hepatocellular carcinoma of the liver.
2—Metastasis to both lungs, the abdominal lymph nodes, and to the serosa of the gall bladder.
3—Portal cirrhosis of the liver.
4—Hemorrhagic ascites.
5—Thrombosis of the superior mesenteric vein, and extension into the portal vein.
6—Hemorrhagic infarction of the jejunum, and the ileum.
7—Marked hypertrophy of the heart, and degeneration of the myocardium.
8—Marked coronary sclerosis, and ancient occlusion of the right circumflex branch.
9—Marked scarring of the wall of the left ventricle.
10—Atherosclerosis of the aorta.
11—Atherosclerotic aneurysm of the right iliac artery.
12—Diverticulosis of the colon.
13—Obesity, and pectoral alopecia.

Discussion:

This case illustrates a multiplicity of pathological conditions. In reconstructing the final picture, one can make the following analysis:

This patient first presented the picture of hypertensive heart disease, and coronary occlusion. The effect of the coronary occlusion, was apparent in the healed scarring of the myocardium, and the thinning of the wall. The failing heart was probably aggravated by the carcinoma of the liver, and the cirrhosis. This induced the thrombosis in the mesenteric vein, and consequent infarction of the bowel. The ascites, was the result of the portal obstruction, and terminal peritonitis. Primary carcinoma of the liver is a relatively rare tumor. It may take the form of a large solid node, occupying the right lobe, or it may assume a multi-nodular appearance, involving both lobes. Histologically, two varieties are recognized. A liver cell type, and a bile duct type. The liver cell type, usually forms cords of large polygonal cells, with pleumorphic nuclei, and resembles the liver cords, while the second type assumes a glandular appearance. The former type has been called a hepatoma, or hepato-cellular carcinoma and is the most frequent of the two. Cirrhosis is often seen associated with carcinoma of the liver. In about 90% of the liver cell type, cirrhosis may

be found, while in the bile duct variety, cirrhosis appears in only about 50% of the cases. These tumors usually metastasize to the regional abdominal lymph nodes, the lungs, and to the branches of the portal vein, as in our case. The infarction of the small bowel presented the clinical picture of an acute abdominal condition. In older people, careful examination of the heart, may often give evidence, that the cause of the acute abdominal condition may be a vascular thrombosis. The prognosis, with resection of the bowel, even in early cases, is usually grave.

Pectoral alopecia is a frequent finding in cirrhosis of the liver. In patients coming to autopsy, 35% of the cases of cirrhosis of the liver presented no hair on the chest, a finding, which at times, may be helpful in diagnosing cirrhosis of the liver.

Summary

A case is presented of a 66 year old man, with a primary carcinoma of the liver with metastasis, associated with hypertensive heart disease, and severe coronary sclerosis, complicated by a mesenteric thrombosis, and hemorrhagic infarction of the small intestine.

* * * * *

"Many cancers of the uterus are due to the fact that the women who bear them have been married to men whose reproductive organs are of disproportionate size. It is evident then, that at each intercourse, there will follow considerable pain and slight bleeding which should be a warning to take precautions."

—The Aphorisms of Corvisart—1818

* * *

"This year the stone-blind shall see but very little; the deaf shall hear but scurvily; the dumb shall not speak very plain, the rich shall be in somewhat better case than the poor, and the healthy than the sick. While flocks, herds and droves of sheep, swine and oxen, cocks and hens, ducks and drakes, geese and ganders, shall go to pot; but the mortality will not be altogether so great among apes, monkeys, baboons, and dromedaries.

As for old age, it will be incurable this year, because of the years past. Those who are sick of the pleurisy will feel a plaguey stitch in their sides, . . . sore eyes will by no means help the sight."

—Diseases This Year; Chapter II
Francais Rabelais—1534

In our drugstore one day a young doctor complained about one of his patients coming to his office so dirty that the other patients in the waiting room would not sit beside him. I jokeingly suggested that the man take a bath. I thought no more of the matter until a few days later a filthy-looking individual handed me this prescription to be filled: Luxis Saponis 1 bar (plain) Sig: Moisten bar in hot water and rub in briskly over entire body. After allowing paste to remain for five minutes, wash off with warm water. Repeat for seven nights then continue treatment two or three times weekly, putting on clean clothes each morning. Dr. ....."

Back in the prescription room, I put a cake of Lux soap — with the wrapper cut off — in a pill box, with the directions.

Two weeks later a cleanly scrubbed young man walked briskly into the store and handed me the box for a refill. When I brought out the second bar, he remarked, "that there young doctor is mighty fine. He told me that I just needed one of them treatments like they give at Hot Springs that I could give myself. Derned if it ain't working; I ain't felt so good in years."

—Mrs. J. M. Kinser (Kingston, Tenn.)
—Life in These United States; The Reader's Digest, January, 1947.

* * *

Boys Will Be Boys

The mother of a small boy with a stubborn case of thumb-sucking thought she would scare him out of it by telling him that if he didn't stop he would get a big, fat stomach.

Soon after she took the boy on a trolley trip. He was sitting quietly when a young woman about eight months "gone" boarded the car.

Then Junior spoke up. "Ooh!" he cried, pointing at her, "I know what you've been doing."

—Clinical Medicine Vol. 53, No. 11, Nov. 1946.

* * *

". . . we doctored the ((wounded)) *horses by searing their wounds with the fat from the body of a dead Indian which we cut up to get out the fat . . ."*

—True History of the Conquest of New Spain by Bernal Diaz, a soldier under . . . Cortes (1519-1521).

* * *

"He boasts of healing poor and rich
Yet is himself all over itch."

—Ancient Greek saying (anon.)

ALUMNI NEWS

First Post War Alumni Meeting

On Wednesday evening, Dec. 4, 1946, at Chicago's Congress Hotel, the first post-war meeting of the Alumni Association of the Chicago Medical School was held.

After a brief presentation on the progress made since the last meeting of the Organization, Dean Sheinin presented Mr. Lester N. Selig, Chairman of the Board of Directors. Mr. Selig expressed his pleasure in meeting with the Alumni and brought them up to date concerning his plans and efforts for the future of the institution. He further stated that there is a place for the school in the educational system of the United States, and that is perpetuation as a great institution is well justified academically and sociologically.

After a brief discussion and question period, Dr. Sheinin appealed for the economic support of the Alumni. The response was spontaneous and the subscriptions were led by Drs. Clinton Elliot and Odis Little each with $5,000. Total subscriptions during the evening amounted to about $60,000; unfortunately, the meeting was interrupted by direction of the Fire Department because of a fire in the hotel.

During the course of the meeting new officers were elected to head the organization.

Dr. Henry A. Smith '31 was elected president, to succeed the retiring Dr. Clinton Elliot '22.

Dr. Henri L. DuVries '25 was elected Vice President; Dr. Morris Fox '39, Secretary; and Dr. Frank Lawler '39, Treasurer.

Dr. Ralph C. Rudder '43 was appointed Chairman of the Endowment Committee of the Alumni Association.

Mr. Selig Meets With New York and New Jersey Alumni

Mr. Lester N. Selig, Chairman of the Board of Directors, was host to Alumni from New York and New Jersey at a Cocktail Party, held in New York City's Ritz-Carleton Hotel on December 15, 1946.

Mr. Selig and Dean Sheinin spoke to the group, which subscribed $20,000 for the Guarantee Fund of The Chicago Medical School.

At the party Dr. Frederick Spector of Brooklyn, New York, was elected temporary chairman of the Easten group of the Alumni Association.

Mr. Mark Sugarman

AN ANGEL IS BORN

During a meeting which was held in New York City, at the Savoy Plaza Hotel on December 11, 1946, Mr. Lester Selig, Mr. Mark Sugarman, and Dean Sheinin addressed a gathering at which a considerable amount of money was raised for the Guarantee Fund of The Chicago Medical School. The highlight of the evening, however, came when Mr. Sugarman startled everyone present by announcing his own contribution of $50,000—by far the leading individual contribution to the growth and progress of our college to date.

1923—The Quarterly received a generous gift from Dr. Mary F. Waring. Thank you Dr. Waring for your contribution and congratulatory words concerning the progress of our school.

1939—The Quarterly was pleased to be notified by Dr. Leon M. Hart of the change of location of

(Continued on page 22)

Faculty Notes

Dr. Sophie A. Nowakovsky

ALTHOUGH Dr. Nowakovsky has been with us since the beginning of the fall quarter, the Quarterly, and so the Chicago Medical School, take this slightly belated occasion to welcome her most whole heartedly into our midst. As an instructor in Pathology and in Clinical Pathology, the sophomore class has already had the fortunate experience of studying with her.

A native of Russia, Dr. Nowakovsky began her medico-pathologic career at the Women's Medical College of the University of St. Vladimir in Kiev. During this time and for a number of years following her graduation, she did much work at the neighboring Pathological Institute. From here, she moved on to Vienna, where, under Chiari, she took her post-graduate work in medicine and pathology at the Allgemeines Krankenhaus.

Following the first World War, Dr. Nowakovsky came to America under the auspicious circumstance of a fellowship in Bacteriology at Northwestern University working under Drs. Candle and Day. In addition, pursuing her inclination, she did voluteer work in Pathology in the various hospitals throughout the city.

Then, in 1922, at Grant Hospital, she became assistant to the late Dr. Jaffe. Following this very advantageous position, Dr. Nowakovsky became Pathologist and Director of Laboratories at the John B. Murphy Hospital for 9 years. From 1935-1941 she fulfilled the same position at the Women's and Children's Hospital, and also at the Gaston Hospital in Dallas, Texas for 4 years following that. It was in the following year, 1946, that our school was indeed fortunate in inducing her to come here.

A licensed physician in Illinois, she was also certified by the American Board of Pathology in 1938. She has published numerous articles contributing to the furthering of scientific knowledge, among the latest ones being: "Specificity of Fetal and of Adult Human Hemoglobin Precipitant," Arch. of Path. Oct. 1940; "Primary Ovarian Pregnancy," Amer. Jour. of Obs. and Gyn., Jan. 1941.

Dr Novakowsky is a member of American Society of Clinical Pathologists, American Medical Association, American Medical Women's Association, Chicago Medical Society, Chicago Pathologic Society, and Illinois Society of Pathology

We again take occasion to welcome the new member of our faculty, the distinguished Dr. Nowakovsky.

Dr. Paul H. Kopper

ANOTHER new addition to the Chicago Medical School faculty is the Instructor of Bacteriology and Preventative Medicine, Dr. Paul Kopper, to whom we extend greetings.

A native of Germany, he received his degree from the University of Berlin before coming to the United States. Becoming a teaching assistant at the University of California he received his M. A. in Microbiology from that institution. Hopping across country, Dr. Kopper next attended Brown University, where, as a research assistant on a Rockefeller Foundation project, he completed his Ph.D. in Biology in 1942.

The next four years were spent in an atmosphere slightly unlike the one prevalent in universities—the U. S. Army. Following his release from the Army, Dr. Kopper joined the faculty of the Chicago Medical School.

A member of Sigma Xi, Society of American Bacteriologists; and the American Public Health Association, Dr. Kopper has done work on the inheritance of blood groups (of the rabbit) and on bacterial enzymes, which work he is still carrying on.

We take this opportunity then, to extend a hearty welcome to the newest member of the Bacteriology Department, Dr. Paul Kopper.

* * *

Dr. Howard H. Beard of the Department of Physiological Chemistry has been elected a member of the New York Academy of Sciences and the Chicago Nutrition Association.

Dr. and Mrs. Piero P. Foa announce the birth of Richard Paul, on October 7, 1946. It is rumored that there was no requisition involved.

At the first Inter-American Medical Congress, Dr. Rudolph Dreikurs was the delegate of The Chicago Medical School.

We submit that a doctor brought up as a perpetual resident with every luxury at his command and consultants at his elbow is no more fitted to be a professor of medicine or surgery than a monk would be to be a consultant on marital relations.

—N. Y. State Journ. of Med., July, 1946.

—from: Clinical Medicine, Vol. 53, No. 12, Dec. 1946.

* * *

The placebo: *"an epithet given to any medicine adopted more to please than to benefit the patient."*

—Clinical Medicine, Vol. 53, No. 12, Dec. 1946.

* * *

Malaria is an eighteenth century Italian word meaning bad air.

—The Merck Report, January, 1947.

* * *

Dr. Morris Fishbein is accredited with the statement that, as a result of advertising, cosmetic sales have jumped from $40,000,000 in 1900 to $20,000,000,000 in 1946.

—The Merck Report, January, 1947.

IN MEMORIAM

Mr. Edward Hopf

In September 1935 Mr. Edward Hopf became a member of the Board of Directors of the Chicago Medical School. He remained in that capacity for eleven years until his death on September 13, 1946. It is with deep regret that we announce the passing of this man who has been so close to our school for over a decade.

Mr. Hopf was born in 1885 on a small farm west of Blue Island where he grew up and received his education. When he was 19 he became associated with the Union Trust Company Bank where he served for over twenty-one years. His fine qualifications were readily recognized and during this period he steadily advanced. Mr. Hopf was prominent in local finance and real estate and at the time of his death was associated with Paul A. Wilde & Co. He was an especially active member of the Building Committee at the school as well as serving on the Board.

May we express our sincerest sympathies to Mrs. Holf, to his daughter, Dorothy, and to his two sons, George and Edward Jr. We are very proud to have had Mr. Hopf with us.

Dr. Frederick Spector

NEW MEMBERS BOARD OF

Frederick Spector, B.S., M.A., M.D., another alumnus of the Chicago Medical School, has been elected to its Board of Trustees.

Dr. Spector was born on December 3, 1916. He entered New York University before the age of 15, from which he received his B.S. degree. He took postgraduate training in Physics at Columbia University and in 1936 was awarded his Masters.

In the fall of 1936 he entered the Chicago Medical School. During his second, third and fourth years he was prosector in anatomy and received the scholarship from the Board of Trustees both his Junior and Senior years. He was awarded his M.B. in 1940 and after interning for a year at the St. Joseph Hospital in Far Rockaway, New York, received his M.D.

At this time he entered the Department of Anatomy at the Northwestern University where he continued his studies for a Ph.D. This, however, was interrupted by entrance into active duty with the Army Medical Corps in September, 1942.

In February of 1944 he left the States for the European theatre of operations. He participated in four major campaigns and was awarded the Bronze Star for meritorious service. By December of 1945 he was once again a civilian holding the rank of Lieutenant Colonel in the Medical Reserve Corps.

Dr. Spector is at present practicing in Brooklyn, New York. He is married and is the father of a 3½ year old boy—Robey.

On behalf of the faculty and students, The Quarterly welcomes Dr. Spector to the school board.

Dr. Ralph C. Rudder

Dr. Ralph C. Rudder, a graduate of the Chicago Medical School, has been elected to its Board of Trustees. Dr. Rudder graduated from the School

OF THE TRUSTEES

of Dentistry in 1928 and was resident in Oral Surgery in Cook County Hospitals from 1932 to 1933. In 1943 he received his M.D. degree from the Chicago Medical School and interned in the Little Company of Mary Hospital from 1943-1944.

At present he is on the staff of the Little Company of Mary Hospital and the Englewood Hospital. He is also an Associate in the Department of Oral Surgery of the Cook County Hospital. At present his practice is limited to oral and plastic surgery.

Dr. Rudder is a member of the Chicago Medical Society, Illinois Medical Society, Chicago Dental Society, and the American Dental Association. He is also a member of the Psi Omega, Omicron Epsilon, and the Phi Lambda Kappa fraternities.

Dr. Rudder has been a very active member of the Alumni Association of this school and because of his interest and participation in the Endowment Drive at a recent meeting of the Alumni Association he was made Chairman of the Endowment Drive Fund.

We welcome Dr. Rudder to the Board of Trustees.

* * *

Hamilton Moritz Loeb, one of Chicago's outstanding philanthropic and civic leaders, was recently elected to the Board of Trustees. Mr. Loeb was born in September of 1900, the son of Jacob Moritz and Rose Stein Loeb. He attended the University of Chicago Laboratory Schools, the Harvard School for Boys, the University of Illinois and the United States Military Academy at West Point, New York.

From 1919 to 1920 he was a member of the New York firm of Crum and Forster. In 1921 Mr. Loeb was made Vice-President of the Chicago office of

Mr. Hamilton Moritz Loeb

Eliel and Loeb Company and in 1940 president of the same firm.

His activities in various philanthropic and charitable organizations since 1921 were varied and many. He has been on the Young Men's Jewish Council, part of the Jewish Social Service Welfare Bureau, Jewish Charities of Chicago and has also participated on boards of the Jewish Welfare Fund and the Community Fund of Chicago. At present he is the director of the Jewish Charities of Chicago and the Jewish Welfare Fund and the Community Referral Service, Vice-President and Director of the Planned Parenthood Association of the Chicago area. He is one of the real leaders of welfare work and community projects in Chicago.

In 1945 he was made General Chairman of the United Jewish Building Fund for $4,000,000 and in 1946 was made Co-Chairman of Advance Gifts "B" Division of the Community Fund Campaign.

We can readily recognize Mr. Loeb's ability in leadership and organization. His presence on the school board is welcomed by all.

Alumni News

(Continued from page 17)

his new office. Dr. Hart is now located at 1362 W. Belmont Avenue, Chicago, Illinois.

1940—Dr. J. Dennis Freund was recently elected to senior membership in the Illinois Psychiatric Society. At the Society's last meeting, Dr. Freund discussed his experiences in a series of 20,000 treatments in the past four years using electro-shock therapy in a paper, "Electro-Shock Therapy in the Presence of Severe Organic Disease". Described for the first time was a method of repetative fractional shock stimuli, the "fractional summation technique", which was introduced by Dr. Freund.

Dr. Freund is a member of the Department of Psychiatry at the Chicago Medical School.

1942—Dr. Leon M. Rothman, who was recently discharged from the Medical Corps, announced the opening, recently, of offices for the practice of medicine and surgery at 2746 Ocean Avenue, Brooklyn, New York. Best wishes for the future from the Quarterly, Dr. Rothman.

Dr. Ben Gelfand, who also recently returned from military service, has resumed his practice of Obstetrics and Diseases of Women. Dr. Gelfand has his offices at 2953 Eighteenth Avenue, Rock Island, Illinois.

Dr. Victor M. Sobey was released from active duty in the Army in June, 1946. He is now a Resident in Neuropsychiatry at the Veterans Administration Hospital in Lyons, New Jersey, after having recently passed his New York State Boards. Congratulations Dr. Sobey, and best of luck to you.

Dr. George E. Fisher is happy to announce that he has passed the New York and Illinois State Boards—at one crack. He is at present on the staff of the Veterans Hospital at Wichita, Kansas. Good luck to you, sir.

1943—Dr. Holden C. McCraney was a recent visitor at School. Dr. Craney was recently discharged from the United States Public Health service. He is now taking a post-graduate course, after which he will return to the practice of medicine in Chicago.

Dr. Eugene Raicus announces the opening of offices for the practice of medicine at 1467 Sterling Place, Brooklyn, New York. Dr. Raicus was recently discharged from the military service.

The Quarterly was very happy to hear of the birth of daughters in December to Dr. and Mrs. Milton Plafker and Dr. and Mrs. G. P. Dillard Jr.

Dr. William Easton was a recent visitor to the School. He had come to Chicago before starting a residency in Medicine to visit some of his classmates. Dr. Easton resides in West Newton, Masachuetts.

Dr. Oscar Schwartz announces his return from military service and resumption of practice at 5019 Twentieth Avenue, Brooklyn, New York.

Dr. Bernard Lieb has also returned from his service in the Army and has opened offices for the practice of general medicine and surgery at 7550 South Halsted Street, Chicago, Illinois.

Dr. Eber A. Wein has opened offices at 3403 Broadway, Chicago, Illinois. Dr. Wein was recently discharged from the Armed Forces.

Dr. Krantz has announced the opening of his office at 1166 Diversey Parkway, Chicago. He interned at the St. Augustana Hospital and assisted in Internal Medicine for one year.

1944—We were very happy to receive the announcement of the birth of Lauren Paula, daughter of Dr. and Mrs. Martin L. Gecht, on December 31, 1946.

Dr. Leonard Tilkin has recently opened offices for the practice of Neuro-Psychiatry at 55 East Washington Street, Chicago, Illinois.

1945—Dr. Seymour D. Guten announces the opening of his office for the practice of medicine and his association with Dr. Benjamin M. Levin. Dr. Guten has offices at 2335 Devon Avenue, Chicago, Illinois.

1946—The Quarterly is especially happy to hear of the birth of Alan Jeffrey to Dr. and Mrs. Sidney Malitz. Dr. Malitz was a past-editor of this journal. The best of luck Sid!

ALUMNI RECENTY SEPARATED FROM SERVICE

Andrew L. Karabin	CMS 1928
Samuel B. Nuzie	CMS 1931
Lewis A. Hare	CMS 1936
Paul M. Egel	CMS 1938
Eber A. Wein	CMS 1943
Eugene Raicus	CMS 1943
Arthur Howard	CMS 1943
Jacob Siegal	CMS 1943
Irwin A. Halpert	CMS 1943
Bernard Lieb	CMS 1943

It is rumored that Wallace Salzman is engaged. We, who know best, and have foresight, know that when this issue is published, Geraldine will have been his wife for two full weeks.

Anomalies and Curiosities of Medicine

Menstruation has always been a subject of interest. In olden times there were many superstitions concerning it. The ancients believed that menstruation was the means by which the feminine bodily impurities were lost. Pliny said that "on the approach of a woman in this state, must will become sour, seeds which are touched by her become sterile, grass withers away, garden plants are parched up and the fruit will fall from the tree beneath where she sits." He also said that "Menstruating women in Cappodecia were perambulated around the fields to preserve the vegetation from worms and caterpillars." Among Australian natives, women in their menses are forbidden to touch anything that men use. American Indian Squaws were obliged to isolate themselves and were forbidden to prepare food for anyone but themselves. It was believed that menstruating women who stepped astride a rifle, bow, or lance would cause the weapen to lose its utility.

On the other hand in some of the Eastern countries menstruation was regarded as sacred, and the first menstrual discharges were considered so valuable that premenstrual marriages were intoduced in order that the first ovum might not be wasted, but fertilized, because it was supposed to be the purest and best for the purpose. Such customs exist at present in parts of India.

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There are numerous instances of women who have had experience in pregnancy unconsciously going almost to the moment of delivering yet experiencing none of the usual accompanying symptoms of this condition. Crowell speaks of a woman of good social position who had been married 7 years and who had made extensive preparations for a long journey, when she was seized with a "bilious colic". To her dismay and surprise, a child was born before the arrival of the doctor who was summoned on account of her sudden colic and her inability to retain water. Duke cites the instance of a woman who supposed she was not pregnant up to the night of her miscarriage. She was menstruating and was suckling a child sixteen months old. During the night she was attacked with pains resembling those of labor and a fetus slipped into the vagina without any hemorrhage; the placenta came away directly afterward. In this particular case the woman was menstruating regularly, suckling a child and at the same time was unconsciously pregnant.

On the other hand, instances of supposed pregnancy with imaginary symptoms and preparations for birth are sometimes seen. For example, a woman who had several children fell sick with a chest affection followed by an edema. For fifteen months she was confined to her bed and never had connection with her husband during that time. Her menses ceased, her mammae became engorged and discharged a serous, lactescent fluid; her belly enlarged and both she and her physician felt fetal movements in her abdomen. As in her previous pregnancies she suffered nausea. Naturally a suspicion as to her virtue came into her husband's mind, but when he considered that she had never left the bed for fifteen months he thought the pregnancy impossible. The belly continued to increase and about eleven months after the cessation of the menses she had the pains of labor. Three doctors were present and when they claimed that the fetal head presented the husband gave up in despair; but the supposed fetus was born shortly after and proved to be only a mass of hydatids, with not the sign of a true pregnancy.

Gould and Pyle

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A study recently completed by Dr. Harlow Shapely of Harvard, reveals that the American public spends an estimated $100,000,000 a year for flowers for funerals as against $5,000,000 for Medical Research.

—The Merck Report, January, 1947.

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The first apothecary shop in the British colonies is generally believed to have been that of Dr. Otto in Bethlehem, Pennsylvania, which he established in 1752.

HEMOCHROMOGENS AND RELATED COMPOUNDS IN LIQUID AMMONIA

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A STUDY of the preparation and reactions of hemochromogens in liquid ammonia by means of spectroscopy and bio-assay has not been made previously, although the Author has made various studies on the reactions of ammonolyzed and ammonated proteins, protein derivatives and hemin. (1,2,3,4,5). The purpose of the present work has not only been to observe and report the chemistry of hemochromogens in liquid ammonia but also to compare these reactions in liquid ammonia or the nitrogen system to similar ones in water or the oxygen system, where such comparisons might lead to better interpretations of reactions, as was demonstrated by Franklin (6). However, there are certain marked differences in the two systems which should be mentioned now. In the first place hemin is soluble in liquid ammonia and reacts with it to form a hemochromogen. This does not exclude the formation of other hemochromogens, however, as will be shown later. The hemochromogen with liquid ammonia is formed in a neutral solution but at pH 11.0. Hemin is not soluble in water at the neutral point or pH 7.0 but it is soluble in aqueous alkali at pH 8.0 to 9.0 which pH is decidedly more alkaline than a pH of 11.0 in liquid ammonia. The reason being, of course, that the ionization constant for water as determined by electrical conductivity is 1×10^{-14} while that for liquid ammonia is 1×10^{-22}. For example, the following reaction was described by Franklin: Sodium amide $NaNH_2$ is strongly basic in liquid ammonia and is neutralized by ammonium chloride NH_4Cl which is strongly acidic in liquid ammonia. The reaction products are insoluble sodium chloride NaCl and more liquid ammonia. This neutralization took place at pH 11.0.

Experimental

The liquid ammonia which was used at the beginning of this work was dried over sodium by the method of Fernelius and Johnson (7). However, it was found later that for bio-assay or spectroscopy that the conjugates which were prepared in the anhydrous liquid ammonia purchased on the open market (du Pont's or Mathieson's liquid ammonia was used in this work) could not be distinguished from conjugates which were prepared in liquid ammonia which had been dried over metallic sodium. Therefore, the laborious and time consuming drying operation was discontinued. Likewise the hemin (Eastman) was spectro-photometrically identical before and after recrystallization. The plasma proteins (Armour and Company), the insulin (Eli Lilly and Company) and the globin (The Wellcome Research Laboratories) were used exactly as they had been prepared by the manufacturers.

A Gaertner high dispersion spectroscope was used for the spectroscopic studies that were made directly upon compounds and conjugates that were dissolved or dispersed in liquid ammonia. The liquid ammonia and solutes were contained in a small Dewar vacuum flask that was mounted directly in front of the slit of the spectroscope. The stoppered vacuum flask was connected to a mercury seal by rubber tubing to permit the ammonia gas to escape and the entire apparatus was placed in a well ventilated hood, wherein were contained a tungsten lamp and a sodium vapor lamp.

The spectroscopic observations were made with a Beckman Quartz spectrophotometer upon compounds and conjugates which had been previously been dissolved or dispersed in liquid ammonia. The reactions were carried out in Dewar vacuum flasks which were attached to mercury seals. The liquid ammonia would boil away within twenty-four hours and the excess ammonia gas could be removed with a vacuum pump. The dry reaction products were then dissolved or dispersed in various solvents, with the exception of liquid ammonia of course, which cannot be used in a spectrophotometer (as it boils at —33.4° C.) without the use of especially constructed vacuum absorption cells.

DISCUSSION

When hemin is slowly added to liquid ammonia, the colorless solution turns from amber

to sherry, then to pink and finally to cherry red. This cherry red compound we believe is a hemochromogen (ammono-hemochromogen) that is formed by the ammonolysis and/or the ammonation of the hemin by the liquid ammonia. That it is a hemochromogen is indicated by the cherry-red color and by the heavy, wide absorption band appearing in the green spectrum at 555 mμ. That the red compound might be a complex formed by both ammonolysis and ammonation is indicated by Kjeldahl analyses of ammonia treated hemin. Using 610.95 grams as the gram molecular weight of hemin chloride there is an increase of 18.39 grams of nitrogen per g.m.w. when the ammonia treated hemin is left under a vacuum pump or over sulfuric acid in a vacuum desiccator for several hours at 22-24° C. If the sample is kept under vacuo at 90-100° C. for several hours there is an increase of 13.6 grams of nitrogen per g.m.w. of hemin used, but if the sample is first evacuated for several hours, then washed with stirring on a sintered glass filter with water several times, after which it is dried at 101° C. the increase is only 6.05 grams. In other words, the nitrogen peels off as it were, depending upon the treatment used to remove it. The increase of 6.05 grams would seem to be rock bottom for the removal of the added nitrogen without any decomposition of the hemin occurring. This amount is approximately one half of a gram atomic weight of nitrogen per gram molecular weight of hemin. The dried ammonia-treated hemin is brown to black in color. With certain hemochromogens prepared in liquid ammonia, such as hemin and egg albumin, however, the color of the dried reaction product also remains red.

The formation of hemochromogen between hemin and liquid ammonia, however, does not prevent the formation of certain other hemochromogens insitu. For instance, if pyridine, potassium cyanide and sodium tetraborate are added to the hemin ammonia hemochromogen in the same proportion of all the reactants, including the hemin, as was described by Drabkin and Austin (8) in their work, the heavy absorption band at 555 mμ will shift to 540 mμ indicating the formation of the more stable pyridine hemochromogen. After evaporation of the liquid ammonia, a spectrophotometric determination made in water also gives a curve indication a strong absorption band at 540 mμ. As will be shown later, protein hemochromogens will also form in the presence of the ammonia hemochromogen.

One striking peculiarity of hemin, that has been treated with liquid ammonia (ammono-hemin) is its solubility in water at a pH below 7.0, between pH 5.5 an 7.0, while untreated hemin is only soluble in water at pH 8.0—9.0. Another difference is the great solubility of treated hemin in ethylene glycol; the untreated hemin is quite insoluble in this solvent. In regard to spectrophotometric absorption the ammonia-treated hemin (ammono-hemin) dissolved in water at 6.3 at a concentration of 0.1 mg per cc, resembles a cross between the acid haematin described by Newcomer (9), which absorbs strongly at 660 mμ and the free alkaline haematin as given by Heilmeyer (10), which absorbs at 10 mμ, and not at all like its precursor in liquid ammonia (ammono-hemochromogen) which absorbs in the hemochromogen range at 555 mμ. It happens to absorb at 620 mμ, the band extending from 605 mμ to 635 mμ, which is the same level of absorption as was given by Heilmeyer for a blood pigment obtained from clinical cases of "haematin jaundice." The same ammonia-treated hemin (ammono-hemin) dissolved in ethylene glycol, however, absorbs strongly at 600 mμ. The effect of the solvent being used and the pH at which the determination is being made often play an important part in shifting absorption bands. Untreated hemin at a concentration of .006% in aqueous sodium hydroxide at pH 9.78 absorbs at 607 mμ, while supersaturated in 10% sodium hydroxide at pH 11.68 it absorbs at 590 mμ. We checked Newcomer's determination of the absorption of acid hemin at 660 mμ. Our pH was 1.26 determined with a glass electrode. If used as a solvent adjunct, guanidine thiocyanate is added to ammonia-treated hemin in ethylene glycol the absorption band shifts from 600 mμ to 500 mμ.

It was reported previously (5) that hemin reacts with glycine to form an insoluble precipitate in liquid ammonia. Since then it has been found that crystalline insulin also reacts with hemin in liquid ammonia to form a precipitate. As proof that the precipitate was a compound or a conjugate, it was finely dispersed in ethylene glycol which was a suitable vehicle, and it was injected subcutaneously into mice, rabbits and dogs. Bioassays of the blood of these animals showed that the insulin-hemin conjugate would maintain a lowered blood glucose of twice the prolongation

of the insulin controls. This conjugate was named insulin-ferri-hemochromogen originally. Later the name was changed to ammono-insulin-ortho-hemochromogen. The latter name describes better its relationship to the nitrogen system of compounds as revealed by Kjeldahl determinations and by spectroscopy. Later work showed that other proteins would also react with hemin in liquid ammonia to form precipitates of various colors. Spectrophotometric analyses of these conjugates made in various solvents yielded curves that differ from those given by the component compounds. Likewise spectroscopic examinations made in liquid ammonia revealed shifts in the absorption bands. These new synthetic compounds were referred to as hemochromogens.

However, in recent years Fairley (11) and Keilin (12) have reported the existence of a class of compounds or conjugates which in some ways resemble hemochromogens but which they classify as haem-albumins, since they found that only serum albumin or plasma albumin would react with hemin to yield them. They were discovered by means of spectroscopy. For comparison, denatured serum hemochromogen has absorption bands at 528 mμ and 558 mμ while haem-albumin has absorption bands at 540 mμ and 570 mμ, as reported by Keilin, and at 530 mμ and 573 mμ as described by Fairley. Their means of preparation was somewhat different but in any case there has been a shift of both absorption bands toward the longer wave length or red spectrum in the case of the haem-albumins. According to the English nomenclature haem-albumin is prepared from native albumin and haematin (hemin-Cl) and then reduced with sodium thiosulfate; haematin albumin from (hemin-Cl) unreduced and native albumin; parahematin from haematin and denatured serum proteins and hemochromogens from haem (reduced haematin) and denatured proteins (protein hemochromogens). In the present work the term hemin is used to mean porphyrin ferric chloride, $C_{34}H_{32}O_4N_4FeCl$.

When desiccated normal beef plasma (Abbott) is added to hemin in anhydrous liquid ammonia a red flocculent precipitate forms which soon settles to the bottom of the flask forming a red sponge-like material. After the evaporation of the liquid ammonia the red sponge is easily powered, and it is slowly soluble in blood serum and sodium hydroxide forming a red gel. The red gel has absorption bands centering at 530 mμ and 567 mμ. The procedure can be repeated using desiccated egg albumin instead of plasma with dried beef plasma in water as a solvent and the red sponge of egg albumin dispersed as a liquid and not as a gel gives absorption bands at 532 mμ and 565 mμ. If averages of the absorption values as given by J. Keilin for haem-albumin and serum hemochromogen are taken, they come at 534 mμ and 64 mμ, just one mμ less in each case than those found for the red gel. Since haem-albumin is formed from a native protein and a reduced hemin, and a hemochromogen is denatured protein and a reduced hemin, the absorption values of the red gel might be accounted for by a reduced hemin and a partially denatured protein. Liquid ammonia is not ordinarily considered as a reducing agent, except in the same sense that nitrogen gas is a reducing agent for oxyhemoglobin, and the amount of denaturation occurring probably depends upon the protein being used. Crystalline insulin can remain in liquid ammonia for forty eight hours without being denatured as to its biological activity, although its solubility in water at pH values below 7.0 is decreased. The role that adsorption of the hemin by the protein might play cannot be overlooked. Some of these hemin conjugates absorb at 600 mμ when ethylene glycol is used as a solvent and ammonia-treated hemin itself absorbs at 60 mμ in ethylene glycol. However, absorption at 600 mμ did not occur for ammonia-treated crystalline serum albumin hemochromogen dispersed in ethylene glycol, if an excess of the protein was used when the conjugate was made. All proteins do not form a red precipitate with hemin in liquid ammonia; for example globin does not do so. As evidence that the red compounds, which have been prepared in liquid ammonia and which have absorption bands falling between those of haem-albumin and serum hemochromogen are not formed by the transference of ammonalyzed and/or ammonated hemin to one of the proteins found in the serum which was being used as a solvent, and thus form compounds similar to those described by Keilin, we can examine the behavior of the red gel mentioned previously. When some of the red powder of ammonia-treated plasma hemochromogen is placed into a test tube containing liquid human plasma and a small amount of sodium hydroxide, the red powder seems at first to be insoluble.

However, it gradually begins to swell and within a few hours it forms a red gel, which fills the lower one third of the test tube, the upper two-thirds being filled with the amber-yellow plasma. The plasma can be decanted, if desired, leaving the tough red gel intact, and it can be removed easily with a rod or a spatula. When the gel is placed in front of the slit of a spectroscope only the red part of the spectrum is visible. However, some of the gel can be stirred or lifted up into the amber-yellow plasma. In this region above the former interface and below most of the stratified amber-yellow plasma, dark bands can be seen, the alpha or heavier band at 562 mμ and the lighter or more diffuse beta band at 530 mμ. In the region at the top of the tube no bands could be detected. Therefore, an eschelon effect could be obtained by sliding the test tube up and down in front of the slit of the spectroscope. The dispersed gel in the intermediate region did not transfer its color to the surrounding plasma on standing. Therefore, it seems unlikely that a compound exactly like the ones described by Keilin had been obtained. In order to differentiate them from somewhat similar compounds of the water or oxygen system, they might be called ammon-meta-haem-albumins or perhaps better ammono-meso-hemochromogens.

It was stated by Fairley and by Keilin that compounds having the spectroscopic absorption characteristic of haem-albumins had not been obtained with any proteins other than human serum albumin. In the work with liquid ammonia, however, ammon-meso-hemochromogens have been obtained with human albumin, beef albumin and egg albumin. The brick red compounds were also obtained in liquid ammonia with bovine beta globulin, bovine gamma globulin and castor bean globulin. The castor bean globulin derivative slowly formed a reddish-jink gel in liquid human serum globulin (serum from which the albumin had been removed). It gave a general absorption only, however. The bovine beta globulin derivative is soluble in ethylene glycol and absorbs at 600 mμ. The bovine gamma globulin is soluble in water made alkaline with sodium hydroxide at pH 10.8 and in ethylene glycol in which some guanidine thiocyanate had been added. The aqueous product absorbs with a broad band centering at about 580 mμ but hemin itself absorbs with a broad band centering at about 590 mμ at pH 11.7. There is some chance, therefore, that the absorption might be influenced by the liberation of hemin brought about by alkaline hydrolysis. The ethylene glycol-guanidine thiocyanate product absorbs strongly at 500 mμ, but so does ammono-hemin and guanidine thiocyanate dispersed together in ethylene glycol. The fibrin foam derivative is soluble in ethylene glycol and gives no absorption band at 600 mμ, therefore, the ammono-hemin must be tightly held in the fibrin foam derivative. There is a diffuse absorption band extending from 585 mμ to 590 mμ. The fibrin foam derivative could, therefore, be classified as an ammono-fibrin-foam-ortho-hemochromogen. The bovine fibrinogen derivative is poorly soluble in various solvents and gives a general absorption but no specific absorptions. The derivative of ammono-globin and ammono-hemin used in the same ratio as is found for globin and hemin in hemoglobins is slightly soluble in a solvent made up of desiccated human plasma, water and some sodium hydroxide, forming a light red or pink solution. There is a strong general absorption as is usually found in compounds containing hemin but the specific absorptions are weak. There was, however, an alpha band at 580 mμ which checks closely with the alpha band at 578 mμ found in oxyhemoglobin, a beta band at 528 mμ which does not check well with the beta band of oxyhemoglobin at 540 mμ and a gamma band at 465 mμ which does not resemble any band in this region found in oxyhemoglobin. Globin-hydrochloride itself is spectroscopically interesting on account of the very broad and deep absorption band centering at 405 mμ which is far in the region of longer wave lengths for a protein. However, it has another band of less intensity and width at 277 mμ. It is interesting for comparison to note the great shift of this heavy band at 405 mμ toward the red end of the spectrum when hemoglobin is formed, yet when globin reacts with insulin which absorbs strongly at 275 mμ to form globin-insulin (Burroughs Wellcome), the two bands at 277 mμ and 275 mμ seem to reinforce one another forming a wide band which extends from 260 mμ to 286 mμ and centering at 275 mμ, but the heavy band of globin at 405 mμ is not affected.

Insulin differs considerably from other proteins in its reactions in liquid ammonia. Crystalline insulin is soluble in liquid ammonia while other proteins are insoluble or only poorly dispersed. The dry insulin-hemin reaction product is some-

what soluble in water, especially so if some glycine has been added to the reaction flask, forming a reddish-amber colored solution. Insulin does not react with hemin to form hemochromogens having a band or, as with some proteins, two bands lying between 500 mμ and 590 mμ, but instead only one band which is located between 590 mμ and 605 mμ, depending upon the pH and the solvent used. This region of absorption is more characteristic for conjugates of hemin with nitrogenous compounds of comparatively small molecular weight such as choline chloride and adrenalin, when ethylene glycol is used as a solvent. However, insulin, either crystalline or amorphous has a strong absorption band at 275 mμ as was shown by Roffo and Francone (13) who concluded, therefore, that in amorphous insulin, the insulin itself is free and not combined. All proteins absorb in this region of the ultra-violet spectrum, but peptones and polypeptides would do so likewise if they contained amino acids which held the phenyl or indol groups. In its behavior as an ammono compound, insulin reacts as if it were a very large polypeptide or a protein of very small molecular weight. Ammonchemin also has an absorption band at 260 mμ, when dissolved in ethylene glycol, while ammono-insulin-ortho-hemochromogen (ortho because its absorption bands lie close to but do not coincide with the bands for ammono-meta-albumin or ammono-meso-hemochromogens) has a band centering at 257 mμ but more diffuse than the insulin band at 275 mμ and the ammono-hemin band at 260 mμ and ranging from 250 mμ to 264 mμ. This change in the absorption bands is evidence in favor of the formation of ammono-insulin-ortho-hemochromogen. The spectrophotometric evidence is corroborated by bio-assay of the compound in regard to its prolonging the lowering of blood glucose in rabbits. For equal amounts used, in terms of the insulin content, subcutaneous injections of ammon-insulin-ortho-hemochromogen will maintain a lowering of blood glucose of twice or more the duration of plain insulin. The addition of choline chloride, glycine and certain other substances affect the solubility, prolongation of action and stability of the conjugate. In addition, ammono-hemin has a diffuse absorption band which centers at 480 mμ, but when ammon-hemin is converted into ammono-insulin-ortho-hemochromogen this band becomes somewhat sharper and its center shifts to 485 mμ but the changes here are not as great as the affect of ammono-hemin on the insulin band at 275 mμ.

Hemin reacts with a variety of nitrogenous compounds in liquid ammonia, such as adrenalin, nicotinic acid, caffeine, histidine and choline chloride. Adrenalin, as has been shown previously, reacts with certain amino acids, sterols and to some extent porphyrins in liquid ammonia to yield conjugates which when injected intravenously into dogs give a prolongation of elevated blood pressure over that of plain adrenalin. The positive nature of the bio-assays are quite marked, but the spectrophotometric evidence is not so pronounced. The obsorption is general in nature weak band at 540 mμ, which would be in the with some specific absorption in the form of a range of a hemochromogen, and the characteristic absorption spectrum of hemin itself is missing. It is this wiping out of the specific absorption bands, as well as the shifting of old ones or the formation of new ones, that often gives evidence of the formation of conjugates, which, in some cases, can be substantiated by bio-assay.

An interesting theory in regard to the important role played by histidine in the formation of cross linkages between protein molecules and other molecules as hemin in such compounds as hemoglobins and cytochromes has been proposed by Keilin (14). For a comparison as to its activity in liquid ammonia histidine and hemin were allowed to react in this solvent and the reaction product was studied spectrophotometrically using water as a solvent. The absorption curve obtained was a general one and the specific absorptions of hemin were missing entirely. This evidence points to the formation of some kind of a compound between histidine and hemin. However, it was found that nicotinic acid and hemin yielded an almost identical curve so that as far as liquid ammonia chemistry is concerned, the reactions of histidine in this regard are not unique.

It has also been shown by Keilin that caffeine is the only compound which reacts with hemin to give a reaction product having absorption bands falling in the same spectral region as those shown by haem-albumin. Caffeine-haem was reported to have an alpha band centering at 570 mμ and a beta band centering at 540 mμ. Caffeine is essentially insoluble in liquid ammonia, but it becomes quite soluble when some ammonium chloride is added to the solution. If hemin is now added to the mixture the solution turns from

colorless to red and a spectroscopic examination in liquid ammonia reveals an alpha band at 577 mμ and a beta band at 548 mμ. Keilin states that the molar ratio of caffeine to hemin should be twenty to one. Therefore, the following quantities of reagents were used: Caffeine 200 mg., ammonium chloride 150 mg., hemin 4 mg. and liquid ammonia 150 cc. Using these proportions the absorption bands are detectable but weak. When more hemin is added the bands become stronger and remain in the positions stated above. Both bands are diffuse but the alpha band is relatively wider and heavier than the beta band. The alpha band shifts 7 mμ and the beta band shifts 8 mμ toward the red end of the spectrum when the reaction is carried out and the spectroscopic examination is made in liquid ammonia. After the liquid ammonia has boiled off the reaction product remains as a brick red powder. This red powder soon turns to a brown powder when it is left exposed to the atmosphere. The red aqueous solution gives a wide spectrophotometric absorption curve with its center at 576mμ. Thus the two bands at 548 mμ and 577 mμ have combined and shifted toward the longer wave lengths. The brown powder is slightly soluble in water and spectrophotometrically it gives only a general absorption. A suitable name for the red conjugate, as it exists in liquid ammonia, with absorption bands at 548 mμ and 577 mμ would be ammono-caffeine-hemin.

Choline chloride is fairly soluble in liquid ammonia and it reacts with hemin in liquid ammonia to form a compound which is water soluble. This aqueous solution of ammono-choline-hemochromogen absorbs in a wide diffuse band extending from 560 mμ to 604 mμ with its center at 582 mμ. The ammono-choline-hemochromogen is also soluble in ethylene glycol and absorbs with a fairly sharp band at 260 mμ. Choline chloride itself is soluble in ethylene glycol and absorbs with an even more intense band at 260 mμ. The ammonia treatment does not cause a shift in the band at 260 mμ, but it causes a flattening of the sharp curve at that position. Choline chloride reacts with insulin in liquid ammonia to yield a conjugate which is quite soluble in ethylene glycol and it has absorption bands at 260 mμ and 275 mμ. Ethylene glycol itself absorbs very slightly at 275 mμ but the zero setting of the spectrophotometer for the solvent control will nullify this effect. Glycerine which absorbs at 288 mμ can also be used, but ethylene glycol is comparatively a better solvent for these conjugates. The spectrophotometric evidence for the formation of a conjugate is the disappearance of the insulin absorption band at 275 mμ when the ratio by weight of insulin to choline chloride is one to twenty. When the ratio by weight of insulin to choline is one to four, the insulin absorption band at 275 mμ begins to reappear and the choline chloride band at 260 mμ almost disappears. One of the reasons for the preparation of this conjugate was to combine a carbohydrate metabolizing hormone such as insulin with a liquid metabolizing hormone such as chloride and to study some of its chemical and biological properties by means of spectroscopy and bio-assay. Since it is known clinically that choline chloride is slightly hyperglycemic and yet when given to diabetic patients who have fatty liver involvement that it will permit the lowering of the insulin requirements, the behavior of such a conjugate became all the more interesting. When the conjugate dispersed in ethylene glycol was injected into rabbits subcutaneously, a prolongation of the lowering of the blood glucose was obtained. A study of the blood glucose curve showed that the blood glucose fell more slowly than it would have done had plain insulin been used, that the low level of blood glucose obtained was considerably longer than would have been the case with plain insulin, but that when the blood glucose did begin to rise, that it rose more rapidly than is usual with plain insulin. This rapid rise, it would seem, was due to the hyperglycemic action of the choline chloride. However, if the proper amount of hemin was added to the Dewar reaction flask, which contained the liquid ammonia, along with the proper amount of insulin and choline chloride, it was found that the conjugate of ammono-insulin-choline-hemochromogen obtained would give a prolongation of the lowering of blood glucose that twice or more exceeded the lowering obtained by plain insulin and that there was no sharp terminal rise of the blood glucose to normal levels.

A spectrophotometric study of hemin and derivatives of hemin in liquid ammonia is principally of academic interest except where it indicates the formation of new compounds such as ammono-insulin-choline-hemochromogen. When the indicated biological activity of such compounds has been substantiated by bio-assay on experimental animals and it has been shown to

be nontoxic and free of pyrogens it is ready for therapeutic trial. However, the requirements of the Pure Food and Drug Administration and of The United States Patent Office are rigorous and the time elapsing between the original observations and the marketing of the drug is usually a long one. The results obtained, however, are ordinarily worth the efforts expended.

Of more direct clinical application is the use of spectrophotometry in the analysis of body fluids such as blood and urine. Many workers both in the United States and in foreign countries have contributed to this field. Among them Heilmeyer (15) is probably the most outstanding for the number of researches completed and for the review and appraisal of work done in this field by others. It is worthy of note as indicating the cooperation that can exist between research workers and commercial entrepreneurs that his book of 280 pages was published by Adam Hilger, Ltd., one of the most famous manufacturers of spectrophotometric equipment. The third party necessary to complete the triumvirate is the medical student himself who will find that he has been well repaid for his hours of reading spent in the field of spectroscopy.

Summary

1. A study of the preparation and reactions of hemochromogens and certain compounds and conjugates related to them has been made in liquid ammonia. Spectroscopy and bio-assay were the principal methods used.

2. The nomenclature used to describe new compounds and conjugates that are formed in liquid ammonia was adopted primarily from the nomenclature as used by Fairley and Keilin for derivatives of hemin and from the nomenclature as used by Franklin in his studies of the nitrogen system of compounds.

3. A new derivative of hemin and liquid ammonia has been described, which exists only in liquid ammonia and which absorbs strongly at 555 mμ.

4. A compound has been prepared by dispersing liquid ammonia-treated hemin in water and this compound absorbs at 620 mμ, which is in the same spectral region as that found for some compound occurring in the blood of patients suffering from black water fever. The ammonia-treated hemin is soluble in water at pH 5.5 and it is also soluble in ethylene glycol.

5. A new preparation has been made by combining egg albumin with hemin in liquid ammonia. This conjugate absorbs in two bands at 532 mμ and 565 mμ. These bands lie midway between those obtained by other workers for haem-albumin and serum hemochromogen. Only when serum albumin was used were they able to prepare haem-albumin.

6. Caffeine-hemin can be prepared in liquid ammonia and it absorbs at 577 mμ and 548 mμ when it is dispersed in liquid ammonia.

7. Insulin reacts with choline chloride and hemin in liquid ammonia to form a conjugate in which the strong absorption band of insulin at 275 mu is missing, yet this conjugate maintains a prolongation of lowered blood glucose of twice the duration obtained by plain insulin.

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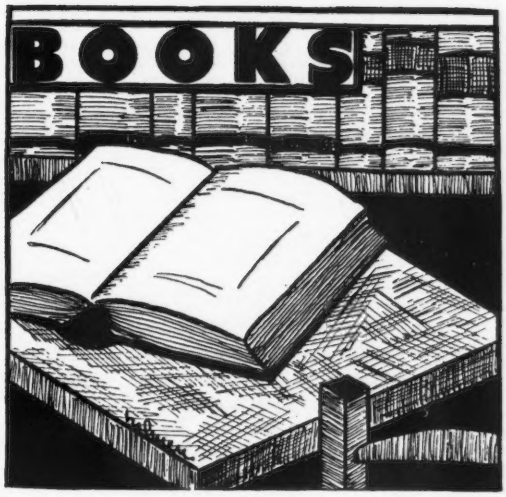

THE CARE OF THE AGED. By Malford W. Thewlis, M. D., Attending Specialist, General Medicine, United States Public Health Hospital, New York City; Attending Physician, South County Hospital, Wakefield, R. I.; Director Thewlis Clinic; Special Consultant, Rhode Island Department of Public Health. Fifth edition, thoroughly revised with 65 illustrations. 500 pp. Cloth, $8.00. St. Louis: C. V. Mosby Company, 1946.

In recent years, medicine has recognized the importance of geriatrics and gerontology. "One of the earliest volumes on old age was written in Latin by Roger Bacon, an English scientist of the 13th Century, and first translated into English in 1683." Many other discussions of the problems, diseases, symptoms, and treatments of old age entities have been presented in journals and books since that time but no integrated and complete manscript had been written prior to this symposium which could be put to good use by the general practitioner.

"The Care of the Aged" embodies not only the direct contributions of six authors but also the indirect contributions of the many friendly and helpful physicians who have, from various parts of the world, corresponded with Dr. Malford W. Thewlis during the past quarter century and who have so generously shared with him the fruits of their experiences.

Until recent years, the physician was not desirous of coping with the problems of senescence and degeneration because there was no rationale in his treatment; he knew little of the anatomic, physiologic, and pathologic changes which occur in the body with the approach of old age. The relationship between nutritional, metabolic, and endocrine equilibrium and the changes occurring during the aging process were not clear in the minds of most practicing physicians. The reactions of old people to infectious diseases are different from those of younger persons. How could one differentiate between senescent changes in the various systems of the body and changes with known etiology?

All these problems which previously handicapped the physician are intelligently and brilliantly discussed in this history and review of the modern advances which intense and open-minded research has brought forth in this 20th Century. * * * * *

THE CHALLANGE OF MARRIAGE: Rudolf Dreikurs, M.D., Professor of Psychiatry of the Chicago Medical School, Chicago, Illinois. First Edition. 271 pp. Cloth, $3.00, New York, Duell, Sloan and Pearce. 1946.

"Writing a book on marriage imposes great responsibilities on the author. Much has been written and much has been read about sex and marriage, not always with benefit to the reader". With these thoughts in mind Dr. Dreikurs has written a brilliant and logical discussion on that which has confused, troubled and confounded mankind since the commencement of gregarious living.

"The Challenge of Marriage" is a challenge not only in title, but in text. The reader is forced to analyze his past actions and deeds because of the realness of the subject and the discussion of problems which have been obstacles to the normal and sound train of thinking of most individuals at one time or other. The delusions which lovers have created for themselves are revealed and the basic elements making for lasting understanding are discussed at length.

The need for such a book must be emphasized with the continual increase in the divorce rate. A sounder psychological foundation for marriage is a needed element in the present attempt of people to live with each other in harmony. The problems of the present day population are many and serious, but with a keener understanding of these very difficulties that cause the emotional anxieties that go with marriage, a world of happier people would be created. When amity truly exists in marriage, the first step towards the making of a peaceful world will have been made.

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Crile & Shivley. Hospital care of surgical patient. 2nd ed. 1946.
Dana, C. L. Peaks of medical history. 1926.
Ford, M... Application of Roschach test for young children. 1946.
Goni, A. R. Myasthenia gravis. 1946.
Graybiel & White... Electrocardiography. 2d ed. 1946.
Guidott, T. De thermis Britannicis tractatus. 1691. Rare book.
Hoskins, R. G. Biology of schizophrenia. c1946.
Key & Conwell. Management of fractures, dislocations and sprains. 4th ed. 1946.
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Spiesman, M. G. Clinical proctology. 1946.
Stefansson, V. Not by bread alone. 1946.
Stone & Dufault. Diagnosis and treatment of pulmonary tuberculosis. 1946.
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Abramson, D. I. Vascular response in extremities. c1944. copy 2.
Adler, A... Inferiority (organ) and its psychological compensation. 1946.
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Carr, C. J. Intravenous sucrose administration. No. 2. 1945.
Directory of Medical Specialists, vol. 3, 1946.
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Ferreira. Dicionario Ingles-Portugues. rev. ed. 1942.
Goldberg, B., ed. Clinical tuberculosis. 2 vols. 1946.
Gotthofer, N. R. Gelatin in nutrition and medicine. c1945.
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Sproull, W. T. X-rays in practice. 1st ed. 1946.
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Thorek, M. The face in health and disease. 1946.
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Vitamins and Hormones. Vol. 4, 1946.
Wenger, O. C. Caribbean medical centers. 1946.
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BURSITIS

At first some twinges near the shoulder joint,
A thing I thought would quickly pass away,
But as the pain increased things seemed to point
Toward its having come for endless stay.
The pain grew worse. I could not use the arm;
To eat, to button clothes brought pain and grief,
Each changed position brought a new alarm
And nothing that was done gave me relief.
No diathermy, x-ray, countless pills,
Nor heat, massage nor hypos helped at all;
Each day and night for weeks a thing that kills
And all of life an agonizing pall.
Of all the things with which I've been acurst
I think deltoid bursitis is the worst.

QUARRELSOME QUATRAINS

Ich liebe dich im winter
For wann es kommt it goes,
Es bleibt nicht to annoy uns,
Vie sleet und ice und snows.

Sophistes, the seer, saith, "My son search not for that which is new for it is not. Remember ye, that which hath been is now, and that which is to be hath already been."

HERPES ZOSTER

A round of golf in bleak autumnal rain,
A chilling of my body to the core,
In two more days a sharp thoracic pain
Intensified each day more and more.
It seemed some fiend had thrust a red hot knife
Within a space upon my tortured chest
A fortnight game me pain enough for life
With scarce a night of sleep or painless rest.
To merely breathe increased the burning pain,
Each therapeutic measure was a flop,
The countless pills I took were all in vain,
I hope that time will bring it to a stop.
When vicious pain with burning intermingles
Why is it everybody laughs at shingles?

* * *

As a result of a meeting held in the pharmacy of Gottlob Bastian, in Dansville, N. Y., the first local chapter of the American Red Cross was organized in 1881.

—The Merck Report, January, 1947.

INDICATIONS FOR SURGERY IN THE TREATMENT OF GASTRIC AND DUODENAL ULCERS: J. William Hinton, Visiting surgeon, Bellevue Hospital, NYC, Bulletin of the N.Y. Acad. of Med., Dec. 1946.

These observations are drawn from a long range point of view of the entire life of an ulcer patient. In the stomach clinic at Bellevue hospital, the policy of medical management of gastric as well as duodenal ulcer has been followed, the former responding more readily. An important question to be considered is the advisability of subtotal gastrectomy to prevent malignant degeneration of a gastric ulcer, considering the high mortality which such an operation carries with the average surgeon and the as yet unproved idea of an ulcer undergoing cancerous change.

Duodenal ulcers diagnosed early respond very well to a medical regimen. A small percentage will become intractable and should be operated on by subtotal gastrectomy; chronic duodenal ulcer with an acute exacerbation should not be mistaken for intractable ulcer, however, and operative results for this are disappointing. Resection plus total removal of the ulcer is also necessary in any penetration with adherence to an adjacent viscus as pancreas, gall bladder, liver, or duodeno-hepatic ligament. Ulcer on the pyloric sphincter gives severe pain and shows pylorospasm on X-ray; this is another indication for subtotal resection and removal of the ulcer.

Massive hemorrhages can be controlled by transfusions and conservative measures. If after receiving 1500-3000 cc. of blood the patient remains in shock, the bleeding is considered arterial and operation is indicated. Elective post-hemorrhage operation is never advised unless uncontrollable pain is present.

In questions as to whether a gastric lesion is a peptic ulcer or a carcinoma, operation is advised.

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THERAPEUTIC "INFORMATION PLEASE": J. A. M. A., 132:16, pp. 963-982, Dec. 21, 1946.

This excellent panel discussion on therapeutics is abstracted here as a brief summary of the latest advances in treatment in the various branches of medical science.

Hematology: (Cyrus C. Sturgis) Folic acid has been shown effective against macrocytic anemias with megaloblastic bone marrow. These include pernicious anemia, sprue, nutritional anemia, and macrocytic anemia of pregnancy, infancy, and post-gastrectomy. I-V or oral radiophosphorus and/or spray x-ray therapy either alone or with phlebotomy in the early stages of polycythemia vera, will keep the blood count normal, in applications at intervals of 6 months to a year or more. Nitrogen mustards, still in the experimental stages, may prove useful for roentgen-resistant patients with Hodgkins disease, leukemia, and polycythemia vera. Cohn's remarkable work on blood plasma fractions opens up a new world of potential therapeutic agents as for instance the globulin fractions specifically concerned with immunity to measles and infectious hepatitis. Rh factor determinations are now considered imperative in all blood transfusions and in all pregnant women. Administration of vitamin K (menadione) to the pregnant woman in the last week of pregnancy will prevent hemorrhagic disease of the newborn due to hypoprothrombinemia. All bleeding tendencies due to hypoprothrombinemia as in obstructive jaundice, may be controlled by parenteral vitamin K, except with associated hepatic disease. Sternal puncture gives a specific picture in 1/6 of hematologic disorders, but an experienced observer must interpret the findings. A blood bank should be part of the equipment of every hospital. Adult males may develop hemochromatosis following multiple transfusions from inability to excrete iron introduced into the vascular system. The great majority of anemias of pregnancy can be controlled or prevented with daily ferrous sulfate given with an average general diet. Death from agranulocytosis should be almost entirely prevented by elimination of the causative drug and prompt administration of adequate penicillin q. 2 h.

Tropical Medicine: (Ernest Carroll Faust) Immunization by employing attenuated P. pestis vaccine has given 80-90% protection among several million people. Typhus immunization with Cox and Castaneda vaccines has greatly reduced morbidity and almost eliminated mortality in typhus patients. In malaria the use of chloraquin promises to be far superior to both quinacrine

(atabrin) and quinine, as both a suppressive and curative drug. Intestinal amebiasis is most adequately treated by use of diodoquin which is, however, slower acting than other iodine compounds. Paraaminobenzoic acid is shown to be relatively specific against the rickettsial diseases of typhus, spotted fever, and scrub typhus (tsutsugamushi). Sulfonamides have proved very satisfactory against bacillary dysentery, cholera, and plague. Cholera vaccine provides 90% protection and lessens the severity of the disease if contracted. Penicillin has proved specific for yaws, pinta, and relapsing fever. Newer, more powerful insecticides than even DDT are now being developed.

Infectious Diseases (Hobart Reimann) Antibiotics hold the stage here and the recent work on streptomycin shows it to be very valuable in specific instances, but not the wonder drug at first expected.

Gastroenterology (Walter C. Alvarez) Dragstedt's double vagotomy for peptic ulcer has proved to be a very valuable therapeutic measure from results as yet obtained on some 200 cases in the last 3 years. The main difficulty thus far encountered is a gastric retention, but the patients gain weight showing adequate intestinal activity. A great simplification advance has been done by Dragstedt in finding an abdominal approach satisfactory.

Endocrinology (Edward H. Rynearson) Thiouracil and propylthiouracil and the use of radioactive iodine represents the latest advances in goitre therapy, but these are under much research and discussion at present. Adrenal cortex extracts and the synthetic desoxycorticosterone acetate have proved valuable but leave much as yet to be desired in Addison's disease. More useful evaluation and more conservative use of androgens and estrogens is recommended. Only specific indications for the use of these drugs should be followed. In certain cases of cryptorchism, gonadotropins are definitely valuable and indicated, but their use in other poorly defined conditions must be condemned. At the present time anterior pituitary lobe extracts have not been proved to be of any therapeutic value.

Cardiovascular Disease (William J. Kerr) Surgery has taken a prominent place in recent cardiovascular advances. In congenital heart disease, ligation of patent ductus arteriosus, end-to-end anastomosis of a branch of the aorta to the pulmonary artery have all been done with success. Proper evaluation is yet to be made before final conclusions are given. Anticoagulants as dicumarol are being recommended in the first 48 hours of an attack of coronary occlusion, but careful laboratory control must be used. Use of large doses of salicylates in rheumatic fever have given no proof of any aid to the cardiac condition.

Virus Diseases (Edwin W. Schultz) Antiviral agents apparently are ineffective since virus infections are intracellular, while bacterial are generally intercellular. Measles is one of the few diseases in which immune serum is of value and then it must be administered early in the disease. Some success has been found, however, with use of antibacterial agents as sulfonamides against trachoma, inclusion blenorrhea, and lymphopathia venereum, while penicillin is of value in experimental ornithosis and psittacosis. Immunization presents a more promising field. Living modified virus vaccines must be used in certain diseases as yellow fever or smallpox, but inactivated virus vaccine is of value in influenza, equine encephalomyelitis, and possibly epidemic encephalitis.

Arthritis (Philip S. Hench) In rheumatoid arthritis chrysotherapy is still on trial and despite its risk of occasional serious reactions, its use is believed justified as the best single treatment now available for a progressive case. In rheumatic spondylitis, x-ray is the therapy of choice but should be combined with postural and deep breathing exercises. Orthopedic advances continue to aid osteoarthritic patients. Rheumatic fever treatment with intravenous rather than oral use of salicylates has not been shown to be in any way superior. Prolonged daily administration of sulfonamides has reduced to 1/6 the chances of acute exacerbation of rheumatic fever over those without such prophylaxis. Gonorrheal arthritis responds favorably to adequate penicillin administration.

A question and answer discussion of great value and interest follow this report.

* * * *

Abnormal Elasticity of Skin

In some instances the skin is affixed so loosely to the underlying tissue and is possessed of such great elasticity that it can be stretched almost to the extent of India rubber. There have been individuals who could take the skin of the forehead and pull it down over the nose, or raise the skin

of the neck over the mouth. In 1888 there was an exhibitionist named Felix Wehrle, who besides having the power to stretch his skin could readily bend his fingers backward and forward.

Gould and Pyle

Albinism

Examples of the total loss of pigment occur in all races but particularly is it interesting when seen in Negroes who are found to be absolutely white but preserving all the characteristics of their race. Rene Caille in his "Voyage a Tombouc-ton" says that he saw a white infant, the offspring of a Negro and Negress. Its hair was white, its eyes blue and its lashes flaxen. Its pupils were of a reddish color and its physiognomy that of a mandingo. Buffon says that albinos are quite common in Africa. Being generally of delicate constitution, twinkling eyes, and of a low degree of intelligence they are despised and ill treated by the other Negroes.

Gould and Pyle

Human Horns

Lamprey has made a minute examination of the much spokn of "Hornd Men of Africa." He found that the anomaly was caused by a congenital malformation and remarkable development of the infraorbital ridge of the maxillary bone. He described several cases, and through an interpreter, found that they were congenital, followed no history of traumatism, caused little inconvenience, and were unassociated with disturbance of the sense of smell. He received no information tending to prove the conjecture that the tribes in West Africa used artificial means to produce the anomaly.

Gould and Pyle

Bearded women are not at all infrequent. Hipprocates mentions a female who grew a beard shortly after menstruation had ceased. It is a well recognized fact that after menopause women become more hirsute.

Gould and Pyle

The prolongation of the coccyx sometimes takes the shape of a caudal extremity in man. Virchow received for examination a tail three inches long amputated from a boy of eight weeks. Ornstein, chief physician of the Greek army, describes a Greek of twenty-six who had a hairless tail, free only at the tip, two inches long and containing three vertebrae.

Gould and Pyle

Displacements of the heart are quite numerous. Deschamps of Laval made an autopsy on an old soldier which justified the expression, "He had a heart in his belly". This organ was found in the left lumbar region; it had, with its vessels, traversed an anomalous opening in the diaphragm.

Gould and Pyle

Cameron describes a child who at birth weighed 14 pounds, at twelve months she weighed 69 pounds, and at seventeen months 98 pounds. She was not weaned until two years old and she then commenced to walk. The parents were not remarkably large.

Famine—An Old Medical Problem

Today famine is a desperately serious problem in many parts of the globe. Famine has played its macabre role down through the ages, presenting problems similar to those of today.

In 1785 in Central Mexico, for instance, a dry season coupled with a great hail storm completely destroyed the corn crop. As with some famines today, the difficulty was basically economic as grain could easily have been brought in from other provinces. The average rural Mexican, however, depended on his land for his sustainance because the wages he might earn were not sufficient to purchase enough food for his needs. The famine, thus, was not one to cut off the food supply of rich and poor alike, and the great increase in utterly destitute people from the lower social levels lead to such an increase in begging, steal-

ing, prostitution, robbery, murder and rape, the police could hardly cope with the problem.

The proposed measures to remedy the situation followed lines similar to those of today. They included public works programs and the purchase of food by the civil authorities. In the city of Guadalajara, for example, municipal kitchens fed two thousand people daily for months.

As with present day famine, concurrent diseases presented a serious problem and typhoid, dysentery, pneumonia and influenza reached epidemic proportions. As hospital facilities were inadequate, rather than permit the victims to die on the fields and the streets from sickness and malnutrition a "provisional hospital for needy paupers, beggers, idle vagrants and foreigners" was set up and called the Hunger Hospital.

It was rapidly filled to its capacity of 240 patients and difficulties soon arose similar to those of any such hastily undertaken relief measures. They included such problems as lack of qualified administrators, difficulties in securing adequate drugs and supplies, the accompanying problem of judicious dispensation of them, and trouble in enlisting sufficient medical help. This was so much the case that it was suggested that physicians be compelled by the governor to take shifts in the hospital. This request for compulsory socialization was not however acted upon. The behavior of the inmates likewise presented a problem as they showed small appreciation for the efforts in their behalf, those recuperating refusing to do allotted tasks, stealing and manifesting a good deal of discontent.

When the famine had passed, the hospital was quickly abolished. But this evidence of inadequate hospital facilities led to the building of a new permanent hospital the next year.

—J. H. U. Hist. of Med.

* * * * *

Celsus and Two Schools of Medical Thought

In all fields where hypothesis rather than knowledge is the order of the day, opposing schools of thought arise. The Roman Celsus wrote of the two principal opposing schools of medicine existing in his time.

The schools were the Rational and the Empirical. The follower of the rational school believed that a knowledge of the hidden causes of disease and of the internal parts as necessary to the practice of medicine. They thus advocated dissection as a means of exploring for the origin of pain and disease, and a knowledge of the action of the body was considered essential.

The empirical school took a more directly practical stand. For example, it denied the value of dissection on the grounds that the characteristics of the organs could not be the same in dissected and whole bodies. They apparently were discouraged by the medical theorizing of their time as attested to by a remark by one of their ranks that "where words abound, the knowledge of healing is deficient." They accepted the need for inquiry only into the evident causes of disease and discouraged research into hidden causes and natural actions on the basis that nature could not be comprehended.

It is interesting to note that the two schools disagreed only in principles, but used identical methods in practicing the medicine of their day.

—J. H. U. Hist. of Med.

* * * * *

AGE

Our young manhood seeks love and craves conflict
And it asks for life rugged and fast.
His emotions preemptory edict,
With scant thought of the future or past.
While in middle life man longs for riches
And positions of highest degree,
Lust for power and wealth so bewitches
Often these become all he can see.
But an old man wants life that is tranquil
And his only desire is for peace,
All activities then are at a standstill
Waiting death that will bring his release.
You can't guess a man's age nor come near it
Merely counting longevity's toll,
For a man is as old as his spirit
And his age is the age of his soul.

* * *

I'd hate to be a sailor
And sail upon the sea,
I'd rather be Norwegian
And ski and ski and ski.
And yet I would decree, sir,
To which you will agree,
That each do what he chooses,
Including you and me.

* * * *

MIDDLE AGE

We're victimized by Fate in every way;
Our girth's becoming greater every day;
Our vision is bi-focal
Our hearing is more local,

The hair upon our pate is getting gray.
Our breath is now quite short, we can't go fast;
We care much less for sport than in the past;
Gone is our shapely figure,
Our bald spot's getting bigger,
We're sharper with retort—iconoclast.
Blood pressure now precludes activity;
Three chins are arguments 'gainst dignity;
Flattened feet have lost their spring,
And we growl more than we sing;
Yet how each one resents senility!

* * *

William Cowper (1656-1709), a London surgeon and anatomist, was, in 1705, the first to report a morbid change in the aortic valves; . . . aortic regurgitation . . .

* * *

The Doctors, tender of their fame
Wisely on me lay all the blame.
"We must confess his case was nice;
But he would never take advice.
Had he been ruled, for aught appears,
He might have lived these twenty years;
For, when we open'd him, we found
That all his vital parts were sound."

—Swift; Verses On His Own Death.

* * *

As late as 1850 . . . a writer in the Medical News and Library remarked, with misguided pride, of the Pennsylvania Hospital: "Anesthetic agents have never been used at a single surgical operation in that institution."

—Med. News and Libr., Phila., 8(May 1850)38.

* * *

In 1885 *James Leonard Corning injected cocaine in or around the spinal canal, producing "spinal" Anesthesia.*

—Surgical Anesthesia, 1846-1946 by Josiah Trent
—Journal of the History of Medicine and Allied Sciences, Oct. 1946, Vol. 1, No. 4.

Coffee contains ½ to 2 grains of caffein per cup; Pepsi-Cola 1 1/5 grains; Spur ⅞ grain; Coca-Cola ½ grain; tea, ¼ to ½ grain; Sanka, ⅛ to ¼ grain.

Patients who drink large amounts of coffee have headaches, confusion, ringing in the ears, flashes of light, pounding of the heart, tremor and insomnia. Persons with peptic ulcer are often aggravated by coffee, tea, or a cola drink.

—S. Med. and Surg. Meeting, 1946.
—from: Clinical Medicine, Vol. 53, No. 12, Dec. 1946.